

DIVISION OF LIFE SCIENCES OFFICE OF
SCIENCE AND TECHNOLOGY
CENTER FOR DEVICES AND RADIOLOGICAL HEALTH FOOD AND DRUG
ADMINISTRATION
5600 Fishers Lane
Rockville, Maryland 20857

MEETING: Epidemiology Research Needs Related to the
Radio Frequency Energy From Wireless Phones

PLACE: The Regal Cincinnati Hotel
Cincinnati, Ohio

DATE: April 18th, 2001

ATTENDEES: Russell Owen, Ph.D. Howard Bassen, Ph.D. Abiy
Desta
Peter Inskip, Sc.D. Quirino Balzano, Ph.D. Mary
McBride, M.Sc. John Moulder, Ph.D. William Lotz,
Ph.D.
Barbara Grajewski, Ph.D. Robert Rinsky, Ph.D. Kenneth Rothman,
Ph.D.

P R O C E E D I N G S

8:30 a.m.

DR. OWEN: I'm Russell Owen from Food and Drug Administration.

I guess the important things I need to remember to mention is that the restrooms are out that door and about three doors down and we will probably go for an hour and a half, two hours right now and take a break for 20 minutes or so and go down and get lunch or do whatever people are going to do at mid-day and then come back after about an hour and half or something and get into the afternoon. We are scheduled to go until 5:00.

A little bit of background for this meeting. Most of you probably know that FDA has been involved in the cell phone and related issues for quite a while and for an even longer time in various radiation issues -- everything from magnetic fields all the way up to ionizing radiation, so this falls in FDA's realm of responsibility.

We have participated in a number of activities over the years, not only our own laboratory research, but various activities to review research and identify gaps in the data and try to help make recommendations for the kind of research that is needed

1 to address these gaps.

2 We are in a cooperative research agreement
3 with the CTIA, the Cellular Telecommunications and
4 Internet Association, that was signed last summer. The
5 reason we have that agreement is that CTIA had funded
6 health-related research for a few years and had a few
7 findings that they were interested in following up and
8 they came to us asking how might we, FDA, and our
9 colleagues in other government agencies help them know
10 what kind of studies they should do.

11 And the positive results that they were
12 most interested in following up, really the only
13 positive results from the program and research, were an
14 isolated epidemiology finding and a series of studies
15 using micronucleus assay.

16 We had a meeting to work on the
17 micronucleus topic last August and came up with some
18 research recommendations. CTIA put out a request for
19 proposals, received proposals. We have reviewed them
20 for scientific and technical merit and given our
21 comments to CTIA on those various proposals and they
22 are in the process right now of negotiating some

23 contracts to do research in that area.

24 So, we have in mind a similar approach

25 here where this is part of our activities to bring

1 input for the kind of studies that FDA might recommend
2 to CTIA under this cooperative research agreement.

3 This is the first of at least two
4 meetings, two planned meetings to bring people in to
5 discuss research that is recently completed, perhaps
6 studies that are ongoing or just beginning and to
7 identify gaps in the data and epidemiology studies in
8 particular -- we really only talking about epidemiology
9 today. And then to try and come up with some ideas of
10 the kinds of studies that would address those gaps in
11 data.

12 If we get far enough along on that, we can
13 talk about the relative priority of those sorts of
14 studies with respect to each, not necessarily in the
15 context of non-epi studies, but really restricting our
16 discussions to epidemiology.

17 In our previous meeting, the micronucleus
18 meeting, we had presentations of research because we
19 were specifically addressing the results from two
20 laboratories, neither of which published their
21 research, so we had to have those people there to
22 present their research so that we could discuss it in
23 detail.

24 We have a different situation here and
25 that is why there are no planned presentations for this

1 meeting.

2 I guess now would be a good time to have
3 people introduce themselves. Near the door we have a
4 draft agenda, which of course, is very simple, and an
5 attendee list, which if you look at it and find your
6 own entry and see that there are problems with it, I
7 would appreciate it if you would mark one up and let us
8 know.

9 Again, I am Russell Owen. I am with the
10 Biology Branch at the Food and Drug Administration,
11 Center for Device and Radiological Health, and I am the
12 principle investigator for FDA on the cooperative
13 research project with the CTIA.

14 DR. GRAJEWSKI: Barb Grajewski. I am the
15 epidemiology section chief of the Health-related Energy
16 Research Branch of NIOSH in Cincinnati. I have had a
17 longstanding interest in non-ionizing radiation health
18 effects, specifically reproductive.

19 MR. DESTA: I am Abiy Desta. I am the
20 technical coordinator for the meetings that take place
21 and I am the one who has been e-mailing you a lot.

22 DR. INSKIP: I am Peter Inskip. I am in

23 the Radiation Epidemiology Branch at NCI. One of the
24 things I work on is a case control study of brain
25 tumors and cell phones is one of many exposures we are

1 looking in that study recently reported on.

2 DR. LOTZ: I am Greg Lotz. I am with
3 NIOSH in Cincinnati as well in the non-ionizing
4 radiation section.

5 DR. BALZANO: I am Quirino Balzano
6 formerly with Motorola. I was part of the team that
7 developed the cellular phone for which we are here.

8 DR. RINSKY: I am Bob Rinsky. I was an
9 epidemiologist with NIOSH for quite a while. A few
10 months back I joined the Surgeon General's Office and
11 became editor of Public Health Reports.

12 DR. MOULDER: John Moulder, a cancer
13 researcher with the Medical College of Wisconsin and
14 also one of the senior editors of Radiation Research.

15 DR. McBRIDE: I am Mary McBride, a cancer
16 epidemiologist at the BC Cancer Agency in Canada. I
17 worked for quite a while in power frequency EMF and was
18 also part of the Royal Society of Canada this year.

19 DR. OWEN: Ken Rothman is expected to
20 arrive later this morning, as is Howard Bassen from FDA
21 and we are fortunate enough to have a transcript being
22 produced of the meeting, so anybody who is interested
23 in getting that later, let us know. Contrary to what
24 the Federal Register notice says, it won't be necessary
25 to go through FOI request to get a copy of the

1 transcript, because we anticipate having an electronic
2 file that will be simple to e-mail to people, so you
3 can just contact me directly if you want that.

4 Before we came here for this meeting, Mr.
5 Desta prepared for us excerpts of three relatively
6 recent efforts to prepare research recommendations. As
7 I said earlier, this is sort of another step in the
8 kind of activity we have been participating in for some
9 time and I thought it would be useful for us to have in
10 mind the kind of recommendations that other groups have
11 come up with recently.

12 I mentioned earlier the WHO International
13 EMF project. The IEGMP is usually referred to as the
14 Stewart Commission in the UK and then we have actually
15 two people in our group that were part of the Canadian
16 Royal Society recommendations, which I guess is this
17 one here -- yes.

18 One thing we should maybe start with in a
19 way to ease into this, is to talk about the kind of
20 studies that have been published recently. As I
21 mentioned, the reason for this effort under the
22 cooperative research agreement is the findings in the

23 Muscat study, which was administered by the WTR and
24 published last December.

25 And, as I am sure you all know, there were

1 not overall findings of associations with wireless
2 phone use in that study, but there was a sub-type
3 association for one sub-type of cancer that was
4 correlated with the use of wireless phones.

5 There has been a lot discussion of that
6 study in the press and some discussion of that study in
7 the scientific literature and actually, I was going to
8 pick on Ken Rothman first, because he recently wrote
9 some very comprehensive review articles that included
10 that.

11 But I would just like to take volunteered
12 information from anybody at the table to comment on
13 that study and what you think we got out of that study
14 and more particularly, what you think was lacking in
15 that study.

16 DR. INSKIP: I take it that the sub-type
17 or sub-category you are referring to is that neuro-
18 epitheliomatous tumor grouping, which as I recall, it
19 wasn't one particular histologic type of tumor. That
20 is a grouping of types of tumor and comes in the ICDO
21 scheme after the code range for gliomas and it includes
22 things like neuroblastoma, neurocytoma, things like
23 that. I don't recall the exact breakdown in their
24 series, but they were treating that as an inclusive
25 category and as I recall, they had an odds ratio of --

1 I guess this is overuse or maybe it was regular use --
2 I don't recall, but of 2.1 or 2.0 and it was a non-
3 significant finding, well below.

4 And in our study, we had roughly similar
5 numbers. In both cases they were small numbers of that
6 category of tumor and whereas they observed
7 approximately a two-fold increase odds ratio, we
8 observed a 50 percent reduced odds ratio, again, not
9 significant. So you put them together and it kind of
10 washes out.

11 I think neither study was really powered
12 to look at sub-type specific associations and when you
13 start breaking down the small sub-groups, you are going
14 to expect things to bounce around and you put our two
15 studies together and that is pretty much what we saw.
16 There is no evidence of a consistent finding emerging
17 from the studies.

18 DR. MOULDER: As I recall, the Danish
19 study did not break out that sub-type?

20 DR. INSKIP: I don't believe it did.
21 Their total numbers of brain tumors in that study was
22 157 or something and that was gliomas and angiomas,
23 everything. With that sort of total number, you would
24 expect the number in this category to be very, very
25 small, so it probably was hidden in that table in one

1 of the other categories. They are lumped categories.

2 DR. MOULDER: That is what I think.

3 DR. INSKIP: Yes. In other statements
4 that have been made in the press -- people have been
5 quoted as saying the reason we should be particularly
6 concerned about this sub-type of sub-grouping of tumors
7 is they tend to occur at the outer edges of the brain
8 and would be potentially more highly exposed to the
9 radiation. I am not a neuropathologist, so I don't
10 know, but just the little reading I have done like in
11 the text book by a world-renowned pathologist, does not
12 make that statement. It refers to them as occurring
13 throughout the brain.

14 So, I think before that observation is
15 given any credence and perpetuated, it should be well-
16 documented from a neuropathologist, because I have not
17 seen that evidence.

18 I actually brought that book and it shows
19 tumors including one category, the neurocytomas occur
20 just that -- centrally. They are in the ventricles and
21 for the gliomas, they tend to occur often in the
22 temporal lobe, but not superficially necessarily in the
23 temporal lobe. They occur throughout the brain, so I
24 really don't know. Again, I would defer to an expert
25 pathologist on that.

1 But I see things mentioned in the press
2 that I haven't seen in the literature.

3 DR. OWEN: Based on your point that
4 neither your study nor the Muscat study was powered to
5 look at that kind of thing, that type of sub-type
6 analysis, just off the bat, is it your feeling that
7 that is the kind of thing that would be needed, that a
8 sub-type -- that studies are needed to do sub-type
9 analysis?

10 DR. INSKIP: Again, I would say I don't
11 think there is anything particularly provocative there
12 as a lead to pursue right now and then you have to say
13 where does the sub-typing end. You can always make
14 finer and finer sub-groups and say okay, but if you
15 look in this sub-group, you will see that -- again, it
16 is indeed molecular. The taxonomy of brain tumors is
17 moving more towards the molecular classification rather
18 than tradition pathological classification. Those
19 distinctions become even greater.

20 So, I would just -- I mean one has to ask.
21 That is a never-ending game and I think you always have
22 to profess a degree of ignorance, but you have to see

23 an end in sight at some point it seems to me.

24 DR. McBRIDE: I would agree with that

25 statement. I think in the face of what we have from

1 the two studies so far, there is no particular reason
2 to look at the neuroepithelial tumors, but the issue is
3 more of power and sub-typing and I would say there is
4 not enough in the biological literature that would
5 point to any particular sub-type at this stage.

6 DR. INSKIP: Just one more thing. Whether
7 when we are talking about the very rare histologic or
8 sub-type of tumor, histologically defined or otherwise,
9 or a particular volume of brain tissue that is getting
10 the highest exposure, it drops off very quickly, so
11 it's a small volume, so even if one was talking
12 hypothetically, of say a doubling of risk of a very
13 rare tumor or in a very, very small volume of tissue,
14 one is talking about a very, very small overall risk
15 and putting together a case series to protect that,
16 i.e., anatomically or histologically, whatever defined
17 sub-type of tumor, and trying to check the likely
18 signal for that relative to other sources of bias, it
19 would be a challenge, I think.

20 DR. OWEN: Maybe a little more broadly, if
21 people would like talk about case control studies in
22 general and what kinds of needs you think we might have
23 here and then we can move on to cohort studies.

24 DR. McBRIDE: Again, Peter, you brought
25 this up in your review and others have as well. One of

1 the biggest issues is exposure assessment and I think
2 before one launches another large study, we need to
3 look at validity studies, self-reporting of billing
4 records and whether or not there are any other
5 approaches that can be used, not that I can think of
6 too many at the moment.

7 The issue of self-reporting and bias after
8 a diagnosis is of some concern -- for example, looking
9 at laterality, questions of laterality of use. This
10 might need to be done before another large study is
11 undertaken.

12 I think also as has been mentioned, the
13 technology has changed and we know in earlier studies
14 we have had a limitation of the numbers of years of
15 use, as has been mentioned -- prevalence of use wasn't
16 nearly as large as it is now.

17 We need to look at power considerations
18 and relevance of the data we could get from a study
19 now.

20 DR. INSKIP: Yes, bear in mind that there
21 is this large IARC coordinated series of studies,
22 depending on which centers all come on board, it
23 remains to be determined, but it's going to be much
24 large than anything that has gone on so far -- in
25 countries where they tended to start heavy cell phone

1 use earlier than they did in the states, so it will be
2 in a much better position than any of the studies
3 published to date to address some of these -- not
4 extremely long latency, but at least clearly longer
5 than what we have and will have very good power. I
6 mean, one can make the argument that there wouldn't be
7 a strong reason to increase, have another whole series
8 go into the field right away. If anything, case
9 control studies should be delayed at some point, I
10 think, so they can deal with a longer latency issue.

11 DR. McBRIDE: I would agree. It would be
12 very useful to get the results of some of those studies
13 before planning another or to identify those areas that
14 are not being addressed in the IARC study, perhaps
15 other outcomes.

16 DR. MOULDER: On the other hand, I think
17 as you look at longer and longer latency, the exposure
18 assessment is going to be more and more difficult to
19 do, because you are either depending on billing records
20 that may or may not still exist or people's memories,
21 which may or may not still exist, on top of the changes
22 in technology.

23 So, that one could -- you could gain a
24 longer latency and longer exposure and then get bitten
25 by poor exposure assessment.

1 similar? I just don't know.

2 DR. McBRIDE: I would think a pooled
3 analysis or a parallel analysis would be more
4 appropriate given the differences.

5 DR. INSKIP: I believe the Muscat study
6 and our study were more similar in design than I think
7 either ours were to the Swedish study.

8 But ultimately the limiting thing is going
9 to be -- whatever categories we use, whatever
10 definitions we use, we are going to run into the
11 roadblock that each study has relatively small numbers
12 of people who have used them for a long time -- more
13 than three to five years, so the numbers get small, so
14 I think however we group the numbers, it's still going
15 to have that in them and even our odds ratio estimates
16 for that are below one even for the heavier use
17 categories, so I am not sure whether putting the
18 results together in sort of a pooled analysis will tell
19 us something that we don't know now or not.

20 DR. OWEN: You have pointed out that as we
21 get a longer term study that better addresses the
22 latency issues, we might run into even worse problems

23 with exposure assessment.

24 DR. MOULDER: You also run into a problem

25 if you wait too long trying to assemble a control group

1 of non-users.

2 DR. INSKIP: Yes.

3 DR. MOULDER: It sounds like a joke, but
4 it's not.

5 DR. INSKIP: No, sure.

6 DR. OWEN: One thing that came to mind
7 that is maybe is more of a pathology sort of question
8 or at least an etiology question for the type of tumors
9 that we are talking about, how long does one reasonably
10 need to look to think that one has -- if you were just
11 going to optimize for the latency question, how far
12 out, how many years of use would you target?

13 DR. MOULDER: I don't know whether it's
14 years of use or latency, but if I remember the
15 Hiroshima-Nagasaki data, brain tumor did not come up in
16 excess until I think 20 years post A-bomb -- 20 or 25.
17 But it's still in excess now.

18 DR. INSKIP: But I don't know if ionizing
19 radiation should be our model for this or not.

20 DR. MOULDER: It's one of those major
21 causes of brain tumors that is even passably
22 understood. I think the ionizing just says it is
23 conceivable that there could be a very long latency.

24 DR. McBRIDE: I guess it depends on
25 whether you postulate an initiating effect or a

1 promoting effect. It's -- we can have the same
2 argument to say that energy levels are not sufficient
3 to really consider an initiating effect as being a
4 well-substantiated hypothesis, but at this point, with
5 so little data, one probably cannot discount it either.
6 So, probably a 20-year life period would be the kind of
7 time period you would be looking at for initial
8 effects, but if we are looking at promoting effects, we
9 would not need as long a latency to say that biology is
10 not telling us enough to know where we should be
11 looking exactly.

12 DR. INSKIP: This is a general area where
13 it seems cohorts would have a clear advantage. If one
14 could set up cohorts with a mechanism particularly
15 updating exposure, level of use and then get
16 infrastructure in place for longer term follow-up, that
17 would seem potentially advantageous both for monitoring
18 a number of health outcomes and in dealing with some of
19 the other challenges.

20 DR. MOULDER: That brings up the very
21 awkward question of whether a cohort study can be done
22 in the United States in the current legal climate.
23 Basically your cohort study was stopped by a lawsuit or
24 effectively stopped. Would anybody dare start a new
25 one?

1 DR. OWEN: I have thought about this issue
2 and I don't want to -- as I said, I think we have
3 plenty of time for discussions, so I don't think it's
4 necessary to really restrict things, but it's not clear
5 to me that that is the core scientific issue of
6 identifying the data gaps and the kinds of studies.
7 Then, I think it's almost a separate activity to worry
8 about the logistics.

9 But, it's true at the next step that that
10 factor can't be ignored.

11 DR. ROTHMAN: Anyway, I think there is a
12 way to do it. The way I would propose to do it would
13 be to enroll people in the cohort as cohort volunteers
14 as has been done in many other cohort studies. I think
15 that averts most of the legal challenges.

16 DR. OWEN: Would it be a challenge to get
17 a large enough cohort if you were doing that?

18 DR. ROTHMAN: It's not a challenge that
19 money couldn't overcome.

20 DR. BALZANO: The advantage of the cohort
21 is going forward with this dosimetric data because what
22 is underlying all these previous studies is essentially
23 the dosimetric.

24 DR. INSKIP: Even in the context of cohort
25 studies though, just from reading just from reading the

1 papers that are out there, there has been less than
2 total success in really getting a firm hand on total
3 level of use. It can be used as subscribership, but as
4 I understand, getting the billing or traffic records,
5 if they don't pull them on -- there are challenges to
6 getting absolute minutes of use. In Europe at least I
7 have read there have been challenges to that. One can
8 make prospective arrangements, I guess.

9 DR. ROTHMAN: I think there are ways to
10 handle it. For example, if we are thinking as to the
11 kind of study that you might do, since you are talking
12 about enrolling people into a cohort who are
13 technologically savvy, I think you could interview them
14 directly or give them questionnaires to fill out
15 directly about their actual use and you can do it
16 through web-based access.

17 You can enroll people who are have
18 convenient web-based access and there will be enough to
19 form these cohorts and it would be a simple matter
20 through e-mail or logging into a special website after
21 they are enrolled in the study, to give you the kind of
22 use information you need for periodic updates.

23 You can get it more frequently than you
24 would need it. I think you would probably not need it
25 more than once or twice a year.

1 DR. INSKIP: So, it's still a
2 questionnaire based approach, but not requiring relying
3 on long term memory or relying short term current level
4 of use.

5 DR. ROTHMAN: Right, especially if you are
6 thinking of following a group for up to 20 years.
7 Aside from whether or not that is necessary, I think
8 you could get use patterns early on and then track them
9 over time at six-month or 12-month intervals. I like
10 six-months because I think you need to keep in touch
11 with the people in the cohort to keep them involved in
12 the study more than you need to get information from
13 them.

14 DR. OWEN: I'm sorry to interrupt, but the
15 transcriptionist is having difficulty hearing people,
16 so if people could speak up a little bit, it would help
17 us get a better transcript.

18 DR. MOULDER: So, your idea is when you
19 enrolled them, you would do the best you could at
20 getting their previous history and the ones in cohort,
21 you would get almost real time information.

22 DR. ROTHMAN: That would be one way to do
23 it. I mean, it would be hard to enroll new users, so
24 you would probably need a history of use before that
25 time. But, you know, if you make an analogy with a

1 cohort study of smokers, what you would do in the same
2 study I think would be to get a history of smoking, but
3 then get continuous information going forward.

4 Now, smoking is a kind of exposure that
5 probably doesn't change as much over time as the
6 exposure that we are discussing, so it would need more
7 updating information as you go. The technology itself
8 is changing rapidly enough to warrant continual contact
9 with the cohort, but contact is also the way to find
10 out about outcome.

11 I think the way to do it is through web
12 access because you can do it at low expense and you can
13 get the information that you need very readily and in
14 computer available format, so that would reduce the
15 budget requirements for a study like that.

16 DR. MOULDER: A theoretical question. Do
17 you think there are enough web-savvy people out there
18 who do not have cell phones that you could get a
19 control group that way?

20 DR. ROTHMAN: Well, you don't have to
21 enroll people who don't have cell phones. You just
22 have to enroll people who don't use their cell phones
23 very much. I have one and I have made two calls in the
24 last year. Those are about the number of days my
25 daughter has let me see it. So, I could be in the

1 study and I would be a non-user.

2 DR. RINSKY: A little earlier we had a
3 comment by Dr. McBride that we need validity exercises
4 here for anything -- any information that comes from
5 questionnaires, so on. I would be very uncomfortable
6 with anything that -- even if it's web-savvy people and
7 so on, until I saw some evidence that this information
8 is reliable.

9 For me, for instance, it's not a memory
10 problem. It's an irritation level with answering
11 surveys two or three times a week, which I get hit with
12 and many other people do as well. If there were some
13 way -- and I don't understand the difficulty with using
14 billing data for volunteers to at least validate
15 questionnaire data, but I don't know why it couldn't be
16 used entirely as long as people are voluntarily
17 complying by enrolling in the study.

18 DR. ROTHMAN: Take my bill for example.
19 The 500 minutes a month that my account is budgeted are
20 all used by my daughter, even though it's my bill. So,
21 you wouldn't know that without talking to me in some
22 way.

23 DR. RINSKY: Absolutely.

24 DR. ROTHMAN: But I think your concern is
25 a good one and one of the principles that you need to

1 use in a prospective cohort study is that you never
2 push hard for enrollment in the beginning. You want to
3 get people who are eager volunteers to start the study.
4 And these are the people who are more likely to be
5 compliant about giving you continuing information and
6 not dropping out of the study.

7 Then you push harder for the updates
8 later. You don't coerce them, but you encourage them
9 as best you can. But you don't do that to get them
10 enrolled in the first place.

11 DR. RINSKY: Interesting point about your
12 daughter. I would suggest that if a person shares a
13 phone that they not be in enrolled in such a study,
14 that that would be one of the initial screening --

15 DR. MOULDER: That would be a killer. I
16 think most phones are shared. A very large number of
17 the phones in existence are shared.

18 DR. RINSKY: That could very well be a
19 killer.

20 DR. LOTZ: I wonder, John, in the sense
21 that the Swedish/Norwegian study of neurologic
22 complaints was constructed primarily based on people

23 who were asked to use their phone by their employer,
24 therefore, given, issued a phone, if you will, they did
25 that because they obviously -- their mission is

1 occupational interest, but they also did it because
2 they wanted people who couldn't say this phone is
3 bothering me, I will give it up. They had to keep it
4 because the boss said I want you to use this phone and
5 I want to be able to call you on it.

6 So, I wonder if even within the very large
7 number of cell phone users whether such a requirement
8 might still be achievable. Obviously it would
9 eliminate a lot of people.

10 Maybe you could sort of partition that a
11 little bit. We have a phone in our family that my wife
12 primarily carries, so the hundred minutes a month, she
13 is probably 90 minutes of that anyway. Once in a
14 while, if I am travelling to get my daughter from
15 college, I will take it and might use a couple of
16 minutes while on that effort, but the sharing is very
17 minimal and actually it sounds like in Ken's case, that
18 would be true also.

19 DR. ROTHMAN: I think the problem is that
20 if you are talking about a long term cohort study, you
21 are going to run into the situation that use patterns
22 will change from time to time.

23 DR. LOTZ: That's true.

24 DR. ROTHMAN: And you can't just drop

25 somebody from the study because they don't meet the

1 study recruitment definition any longer.

2 So, I think that the only solution for a
3 long term cohort study is to broaden the entry criteria
4 so that you can include almost any user, but then keep
5 in close touch with that person, each person, so that
6 you can understand what the use pattern is and how it
7 might change. Other than that, I think the study
8 wouldn't work.

9 DR. MOULDER: Assuming the use pattern is
10 changed dramatically over the last five years and if
11 these various uses of phones turns out to be reality,
12 there are going to be further drastic changes in use
13 patterns.

14 The other reason why billing minutes
15 wouldn't work is the large number of people who have
16 gotten headsets. The billing minutes will not tell you
17 whether they are holding the phone.

18 DR. BALZANO: Yes, that is another issue -
19 - where is the phone? That can change very much what
20 you are looking for.

21 DR. MOULDER: Yes, this started out with
22 validation and I would agree that validation needs to
23 be done, but validation is going to be tough and I
24 don't think billing minutes is the solution. It may be
25 part of the solution.

1 DR. BALZANO: I can inject one
2 technological aspect of it. We are going to have more
3 and more of these phone cards that unites the families
4 of the world. Each one of them gets phone cards, so if
5 they want to use the phone, they insert the card and
6 the phone registers the card and at that point, you
7 know who is using it. This is not far out technology.
8 This is technology that exists. And one criterion at
9 the time of enrollment, just when someone uses the card
10 then at that point, it is identified by the base
11 station by the pay station who is using it. This is
12 entirely feasible. It is not far out technology.

13 So there are technological ways to go
14 around some of these issues. And there is a certain
15 cooperation between the industry you running the study,
16 it is possible to introduce some technology that can
17 help you understand.

18 DR. ROTHMAN: Yes, I think that is
19 certainly an idea that could be explored. The problem
20 you want to watch for, is you don't want to study a
21 technology that is not pervasive. You don't want to
22 focus on something that wouldn't apply to people who

23 are non-users.

24 DR. BALZANO: You are right, but going

25 forward, Ken, the phone is going to be a throw away

1 item. In a short time, the phone is a \$10, \$20 item.
2 You buy the card, insert the card, use it pretty much
3 like you buy the film and throw away the camera. It is
4 going to go down that path more and more, except for
5 eventually the third generation of phones that give a
6 display, in which case, it is not going to be a throw
7 away item.

8 But if you are looking for a talk and
9 listen at the head, that is probably the way the
10 technology is going and at that point, it's the card
11 and everyone gets his own card.

12 DR. MOULDER: But the change in the
13 technology creates even a worse problem. If people are
14 using these phones for web access in the future, they
15 are also not going to be holding up their heads most of
16 the time because they have to look at the screen.

17 DR. BALZANO: As I said, the different
18 between the 3-G and the talk and listen. The talk and
19 listen, the throw away phone, that is the one I was
20 saying --

21 DR. MOULDER: What is ends up meaning is
22 that a cohort study is going to have to be staggeringly
23 flexible at the beginning because you are talking about
24 setting it up to measure exposures of a technology that
25 you don't know where it is going.

1 DR. McBRIDE: It's interesting. I mean,
2 one would have to define those characteristics that you
3 feel will be important characteristics of exposure
4 while accounting for the technology.

5 DR. BALZANO: The technology is the
6 reason. We all agree to that. Second, there is that
7 again -- the technology -- if this is imbedded, the
8 technology is imbedded in the study to begin with
9 instead of trying to catch it at the end, I think we
10 can overcome quite a few of these issues and that
11 indeed -- the phone in the hand, the US might not
12 penetrate that fast because a lot of the US are
13 drivers.

DR. MOULDER: I think this
14 might be a bigger problem for validation. With your
15 idea on the website, you are going to ask them, how
16 much did you use your phone in the last six months or
17 year while holding it to your head as opposed other
18 uses.

19 DR. ROTHMAN: You can ask them for the
20 last week.

21 DR. MOULDER: Yes, okay.

22 DR. BALZANO: If you are performing a
23 forward study, we can put a little capacitor and when
24 you put it to your head, the capacitor switches on and
25 if you keep it in your hand, the capacitor doesn't

1 switch on and it tells you -- I mean, ladies and
2 gentlemen, let's take into account the potential of the
3 technology here.

4 If we are marching without looking forward
5 and inviting some cooperation, I think you are running
6 against a much tougher wall. We know what we want and
7 we ask for some technology advantages.

8 In the European study, the industry has
9 provided Dr. Elizabeth Cardis with dose phones and dose
10 phones tells you which side the customer is using the
11 phone, tells you the person, tells you proximity to the
12 ear, the month, the time it was used, what kind of
13 power level was recorded at the time. There are ways
14 to go around, but I think you have to put it in in the
15 beginning.

16 DR. OWEN: You mention the dose phone
17 component of some of the IARC studies. How large is
18 that component of the study? How many dose phones are
19 there?

20 DR. BALZANO: I think about 100. That as
21 deemed to be statistically sufficient by the
22 statisticians to be enough to find the statistical
23 parameters. This is the number as I recall.

24 DR. McBRIDE: Is it fair to say then when
25 we are talking about exposure measurements in such a

1 cohort study that there are a bunch of technology
2 issues and characteristics of the phone or transmission
3 device and whatever that is is going to change
4 markedly.

5 There is also a set of personal
6 characteristics, how people use their phone, that also
7 needs to be tracked. There may be fewer of those
8 variables. They may not change, but there needs to be
9 some definition of those sets of characteristics.
10 There needs to be an examination of how to capture
11 those characteristics.

12 And as you have said, it may be that the
13 phone technology itself can help to capture some of
14 those and there needs to be some validation of the
15 methods that people come up with to capture those
16 characteristics to move ahead with exposure protocol.

17 DR. BALZANO: I could give a suggestion
18 that if we separate the exposure assessment from the
19 technology studies one from the other, it might help
20 you quite a bit.

21 As we look forward to the technologies are
22 coming down and decide what kind of protocols you are

23 going to be using, just test them out using dose
24 phones, using the technologies available.

25 By the way, I think the US is going to be

1 somewhat different from Europe and Japan. The Japanese
2 (inaudible), so a lot of these third generation devices
3 will work very well. That is why (inaudible) was so
4 successful. It is not clear that the same technology
5 is going to be so successful in the United States.
6 People drive.

7 The technology is advancing very rapidly.
8 This is a window of opportunity to run a good study in
9 the United States before all these new technologies
10 comes in to shed light on the present technology.

11 DR. McBRIDE: Getting away from exposure
12 assessment for a moment, the question, Ken, that I ask
13 since you raised it is the issue of compliance among
14 infrequent users. I can see that probably that could
15 be somewhat problematic, but I think I agree with you
16 that if you throw enough money in there to keep people,
17 you could end up with acceptable participation. In
18 terms of putting it in the first place in compliance --

19 DR. ROTHMAN: Yes, it is a problem. I'm
20 not sure if the problem would depend much on how much
21 people use the phone. It depends a little on how the
22 study is pitched, but there is also inducements as

23 another option. If it's a big study, it's expensive,
24 but it still may be worthwhile.

25 DR. McBRIDE: In supporting, a suggestion

1 that dollars will help --

2 DR. ROTHMAN: Usually that is the case.

3 DR. BALZANO: I can add -- are we
4 restricting ourselves to head exposure or are you
5 looking at present technologies that leave the phone
6 somewhere else on the body? That is a question that
7 should be addressed.

8 DR. OWEN: I think we should not restrict
9 ourselves that way.

10 DR. ROTHMAN: Actually in part to address
11 the previous question, one thing you ought to consider
12 in a study like this is to broaden the cohort
13 definition to make it a study of technology, for
14 example -- technological exposure. Look at -- ask them
15 about the hours that they spend in front of a video
16 display and perhaps some other things.

17 There are various things that you could
18 expand it to at no particular cost to the study and
19 actually of some benefit. For example, people who
20 hardly ever use the telephone might still spend a fair
21 amount of time in front of the TV screen or a computer
22 screen and as long as they are participating in the
23 study of modern technology and its health effects, they
24 may be eager to continue.

25 So, I think that is another approach to

1 addressing the compliance problem and it gives you the
2 benefit of being able to study other technologies as
3 well.

4 DR. OWEN: You are saying that by
5 including assessment of multiple technologies, that
6 will motivate some people to be more compliant with the
7 protocol?

8 DR. ROTHMAN: Because it's easier to make
9 -- you change the pitch. First of all, you have to do
10 that because if you are going to do a 20-year cohort
11 study, you would be derelict if you didn't start asking
12 questions about other exposures that you might easily
13 study. But in that case, you don't have to call it a
14 study of cell phone use, which does present a problem
15 for people who don't really use it very much. They
16 don't understand what their contribution might be.

17 So, you talk about it as a study of the
18 modern environment or a study of technologies in modern
19 life, something like that. And you can make a better
20 pitch I think.

21 DR. RINSKY: That is a very good point.
22 In my mind, that legitimizes doing the study at all.
23 It's really questionable in my mind whether we should
24 be studying cell phones in particular because it's easy
25 enough to change the exposure patterns of that by

1 having people not put it next to their body.

2 So, just on a precautionary principle sort
3 of thing, we don't need the answer to take corrective
4 actions in that particular venue. But if you are going
5 to study all -- if you are going to study human
6 interaction with modern technology, then I think I and
7 others could get excited about that sort of effort.

8 I think around this table we can agree
9 that people shouldn't be going down the road with a
10 phone planted on their head for other reasons as well.
11 It's technology that should be applied anyway.

12 DR. BALZANO: Somehow communication is a
13 repressed need that has been there for quite a while.
14 Otherwise, you would never see this exposure that you
15 are seeing in the last few years and if they are
16 walking down the street and they want to communicate,
17 this phone is not going to be far from them. I think
18 we have to keep in mind that if it is not there, it's
19 going to be somewhere else.

20 So, you cannot separate them too much.
21 You cannot go around with a five-foot long stick -- not
22 even a three-foot long stick. It's going to be pretty

23 close to the body somewhere and that is why I think
24 again that it's worth looking into the matter. What we
25 are seeing is not so much an explosion for the cellular

1 phone industry, but it enabled people to keep in touch
2 with each other for whatever reason.

3 We have to look at the Europeans, for
4 example. There is a mother talking to the son, to the
5 daughters and everybody else in the family. That was
6 the explosion. Nobody knew it was there and now we are
7 seeing it unfold.

8 DR. RINSKY: I'm not exactly sure -- are
9 you taking issue then with what --

10 DR. BALZANO: No, I am not taking issue.
11 I'm saying you don't respect the fact that calls you
12 can place -- you can have an ear pad. Now the phone is
13 not going to be near your body. You are walking down
14 the street and you want to keep in touch, your phone is
15 going to be somewhere on top of you, if not on your
16 body. If it is designed to be at the head and you put
17 it on your body, I am trying to say that exposure might
18 be higher somewhere else than at the head.

19 DR. MOULDER: That one would not be very
20 much fun to study because people seem to wear the
21 phones in a bewildering variety of different places, so
22 you are moving the exposure from the head to an unknown

23 part and highly variable part of the rest of the body.
24 So, even theoretically, the cohort study
25 is going to say if you then have to ask if you are

1 using a body-worn phone, where do you wear it.

2 DR. BALZANO: People have probably have a
3 wearing pattern no more or less than the pattern of the
4 head.

5 DR. MOULDER: But I could see you ending
6 up with about 70 sub-groups very quickly -- left pocket
7 versus right pocket.

8 DR. BALZANO: Or left side versus --

9 DR. MOULDER: Yes.

10 DR. GRAJEWSKI: I have some concerns I
11 guess with the complexity of exposure assessment, what
12 the updates will look like or what the length of
13 updates would be on a cohort study, much less the
14 baseline questionnaire, but would there be some way to
15 simplify updates and exposure assessments on updates so
16 that this wouldn't become an unduly long instrument for
17 people to do, because with a monetary incentive, if you
18 have a really long instrument for them to do on an
19 updates basis, I would start questioning what was
20 coming in perhaps based on whether people lost interest
21 or got someone else to start doing the filling out for
22 them or whatever.

23 DR. ROTHMAN: I agree entirely. I think
24 it would have to be a short update instrument. Maybe
25 the enrollment form could be long enough, but at that

1 point, you do want to use it in effect for screening
2 out people who are not complying. And then once they
3 get beyond that, then I think the interactions ought to
4 be quick and easy.

5 And one technique that you could use in
6 the nurse's health study and the other studies coming
7 out. They send update questionnaires and they ask
8 about different things at different times. They don't
9 always ask the same set of questions. Even so, their
10 periodic questionnaires are much too long, a real pain
11 to fill out. I think you have to keep it brief.

12 DR. MOULDER: Having never done this, what
13 is your feeling of the optimal length for a
14 questionnaire? I don't know whether you are talking 10
15 questions or 200.

16 DR. ROTHMAN: Well, my feeling -- it's
17 just a feeling so I don't know how much it's worth, but
18 I think that what we ought to be talking about would be
19 a 10-minute maximum session at a terminal on a website
20 perhaps filling in some questions. Maybe just a few
21 screens, clicking on things. Things they can do
22 quickly. I mean, with a little time and motion study,
23 I am sure you could get a fair amount of information in
24 a few minutes.

25 I think it would be even better to be five

1 minutes. If it goes beyond 10, I don't think it's
2 going to work.

3 DR. OWEN: And you are thinking of this in
4 terms of having six months or a weekly? Under which of
5 those protocols would you see --

6 DR. ROTHMAN: If there were my study, I
7 would suggest to do that every six month. You send an
8 e-mail to somebody and you say click on this link and
9 go to a site and it comes up with their personalized
10 questionnaire. And you can tailor the questions to the
11 people based on their previous responses with
12 sophisticated enough software. And you just ask them
13 crucial information, update -- you are updating what
14 you need to know and you are staying in touch with the
15 individual. You are saying if you have moved, if you
16 have got a new address, new telephone number, let us
17 know. That kind of thing.

18 That is why you need to make it six
19 months. The post office doesn't forward beyond six
20 months and you want to keep in contact.

21 DR. McBRIDE: Our experience with mobility
22 of patients is that if you don't keep up the file, the

23 longest you would want to leave between contacts would
24 be a year because you do -- you can lose people quite
25 easily.

1 It's an interesting technology. There is
2 a lot of data on the length of interview questionnaires
3 or telephone interview or personal interview
4 questionnaires, self -- mailed questionnaires, but
5 there is not a lot that I have seen on the optimal
6 length of a web-based questionnaire. That would be
7 interesting to follow for other studies.

8 DR. MOULDER: The interval update, I think
9 would need to be something like six months. I have a
10 feeling that e-mail addresses are even more volatile
11 than phone numbers and postal addresses. They don't
12 forward very well.

13 DR. ROTHMAN: Yes, what you would do is
14 when you enroll people, you would get their postal
15 address and their e-mail and you stay in touch with e-
16 mail and if the e-mail turns out to be a dead end, then
17 you write a letter and you say we lost track of you
18 through your e-mail, can you --

19 DR. MOULDER: You don't want to wait a
20 year to do that. So, the interval would have to be
21 something like six months.

22 DR. ROTHMAN: And you don't want to make
23 it more frequent than that because you will annoy them.

24 DR. BALZANO: You can always use the phone
25 also. Ladies and gentlemen, don't forget you have that

1 technology there that can help you out. I hate to keep
2 going back to this issue, but I would like to see at
3 the end of the day that we decide the critical
4 parameters and we use the traditional methods if you
5 want, the nice traditional methods and then we use the
6 technology to the hilt to simplify our lives because it
7 is possible.

8 DR. McBRIDE: Also your point about
9 tailoring the questionnaire and being able to lead
10 people through questions based on their answers to
11 other questions certainly is a good way to --

12 DR. MOULDER: Has anybody actually done a
13 web-based cohort that you know of?

14 DR. ROTHMAN: There have been a couple
15 that I have heard about and I just read a grant
16 application yesterday for a cohort study using web-
17 based access, but it's experimental, so I think people
18 are just dipping their toes into the water right now.

19 But if they are looking ahead, this is
20 certainly the way studies are going to be done.

21 DR. OWEN: You were talking a lot about
22 validation. To me, it sounded like mostly we were
23 talking about validating the -- whatever method -- the
24 questionnaire or the billing record with respect to how
25 well that actually tells you what the use is.

1 And then you were mentioning for instance
2 the dose phone that then allows you to connect any
3 given type of use to what the actual dose rates are.
4 Do you think that if you had some kind of study like
5 this where you were updating periodically and you had
6 all these changes in personal characteristics, that you
7 would need to build in also periodic sub-studies or
8 reassessments to figure out what kind of doses those
9 kinds of changes meant?

10 DR. BALZANO: The answer is yes and I will
11 tell you why. If you are living in town, you have a
12 much higher changes of exposure. You are not
13 necessarily talking to the closest station. It depends
14 on the location of the station. It might be shallow
15 and actually you might be talking to further out than
16 the closest, so the closest station might not tell you
17 that that is the one you are talking to. If you are in
18 the suburb, you might be talking almost always to a
19 further out station.

20 So, what I would like to see if at all
21 possible, indeed to find out what are the patterns,
22 because here they are talking about patterns. We are
23 not anything specific. We want to know someone living
24 in the canyons of New York or somewhere, what is their
25 exposure during the day or some other parts of the

1 country. And there is a very rapid variation of
2 exposure levels. This is not stationary, so I would
3 really like to see that.

4 Again, the collection of some of these
5 data is done in Europe right now and if you contact
6 Elizabeth Cardis as soon as she can provide this does
7 phone information --

8 DR. MOULDER: Even if you did it right
9 now, you would have to do it again in five years or
10 even 10 years because as the technology changes, the
11 patterns could dramatically change.

12 DR. BALZANO: Plus again, the environment
13 in the United States is not the same. Here we have
14 much taller buildings in the center of town where you
15 have more people.

16 Again, what I would like to see is a
17 certain number of parameters that come out of our
18 decisions, the decision in the next week. Maybe the
19 question is to come up with --

20 DR. MOULDER: We started this out talking
21 about case control and then switched to cohort, but
22 switching back to case control for a moment, none of
23 these sort of things as I can see are applicable to a
24 case control study. This sort of information
25 essentially has to be cohort.

1 With case control, the exposure is already
2 there. There is no way you can measure or assess any
3 of these things -- at least no easy way.

4 Any response from those of you who
5 actually do case control?

6 DR. INSKIP: You can ask questions, but
7 interpreting just what those questions mean in terms of
8 translating it to the context of this pilot study of
9 100 measurements of actual exposures, that would be a
10 challenge.

11 DR. ROTHMAN: Case control study would be
12 more valuable if there were a short term effect and it
13 would be most relevant to the possibility of a short
14 term effect, but if you are talking about more
15 induction periods for this kind of exposure, I don't
16 see much alternative to a cohort study.

17 DR. MOULDER: That is what pushed us into
18 talking cohort studies in the first place.

19 DR. INSKIP: Just as one other -- for
20 cancers that have been fairly stable for an extended
21 period of time, not going up or down particularly for
22 reasons we don't understand, one could at low effort
23 monitor through population-based cancer registries and
24 just see if there has been a change -- and I am not
25 advocating doing body counts, but do analytic studies.

1 But there are some sites that have been stable over a
2 period of time and if say use of cell phones increases
3 the incidence by a factor of two or three within a
4 reasonably short induction period, one would expect
5 that to change. And a very low cost sort of thing to
6 do.

7 Now, for some brain cancers or something -
8 - particularly since they are in age groups where there
9 has been a secular trend and debate about the role of
10 diagnosis versus etiology, it would be hard to try and
11 pull out some other factor superimposed on a trend
12 which we don't understand and we will have
13 disagreement. But for something that has been stable
14 for a period of decades, one could look for a sharp,
15 recent change.

16 DR. MOULDER: What is the situation on the
17 gliomas? Is that one stable with time or not?

18 DR. INSKIP: It's been going up in the
19 older age groups. I think most people think that is
20 largely improved diagnosis.

21 DR. MOULDER: Yes.

22 DR. INSKIP: And among younger and middle

23 aged people, it's been much quieter. One possibly
24 could do something there. People for a while are going
25 to look at trends in anatomic location of gliomas

1 versus -- say temporal lobe gliomas versus others, but
2 the problem with that as well is again, this changing
3 technology. Things are getting up in other categories
4 and getting put into premise categories, so there are
5 pitfalls in that sort of analysis as well.

6 DR. MOULDER: Does most registry data
7 contain anatomic location or just diagnosis?

8 DR. INSKIP: It's requested by a lot of
9 registries. I don't know how complete it is for all
10 registries. At least in SEER, I believe it is.

11 DR. McBRIDE: I see there are sort of two
12 issues. One is whether or not it's reported to the
13 registries and secondly the level of detail the
14 registry records.

15 So, yes, in the Canadian data, it shows
16 essentially the same as you just talked about, Peter,
17 but there are those issues of reporting and coding that
18 make the interpretation of that somewhat difficult
19 also.

20 DR. INSKIP: Right, I don't think it
21 answers the question, but it can flag your attention
22 and comes at very low cost.

23 DR. McBRIDE: Yes.

24 DR. INSKIP: Just as a recent example,

25 there was a concern about ocular melanoma and so that

1 is an example of a tumor, which has been over a period
2 of decades fairly flat in sharp contrast to melanoma of
3 the skin, so one perhaps could look. It suggests that
4 there was a threefold risk associated with using
5 cellular phones or walkie talkies and at least very
6 soon one might expect to see evidence of that at a
7 population level.

8 DR. McBRIDE: Yes.

9 DR. INSKIP: That was a study done several
10 years ago, so whatever the induction period, periods of
11 use was at that time, that is what it was and they were
12 reporting an excess risk, so that wasn't possible
13 excess risk in the future. That was a risk at that
14 time.

15 DR. McBRIDE: Another area in case control
16 studies perhaps that we haven't talked about is whether
17 looking again at high exposed groups would help us.
18 The groups that I am aware of are militarily exposed or
19 medically exposed through their occupations.

20 One thing I don't understand enough about
21 is how those exposures are different from cellular
22 phone exposures. I know they are different and I don't
23 know whether the effects seen at some of the different
24 -- the diathermy and other situations are applicable to
25 a population of cell phones users. Again, there are

1 gaps in the dearth of data in looking at the potential
2 effects, it was two similar, but different types of
3 exposures.

4 DR. BALZANO: Diathermy pretty much faded
5 out in the US -- am I correct?

6 DR. MOULDER: Diathermy is getting pretty
7 rare in this country.

8 DR. BALZANO: As far as I know. I know in
9 Canada and the US in the last 20 years, I don't know if
10 there has been very much.

11 DR. MOULDER: What about military though?
12 I know military -- presumably are more powerful. They
13 certainly use a lot of hand-helds. They certainly are
14 physically larger. I assume they are a lot more
15 powerful.

16 DR. LOTZ: You are speaking of walkie-
17 talkie type things?

18 DR. MOULDER: Yes, I don't know if they
19 call them walkie-talkies anymore.

20 DR. LOTZ: I think they generally still
21 do.

22 DR. MOULDER: Those are five or six watts.

23 DR. LOTZ: Two-way radio or whatever.

24 DR. MOULDER: And they do tend for reasons
25 I never understood to hold them differently. They

1 still now tend to hold them here.

2 DR. LOTZ: I'm not sure whether if you
3 wanted to talk about two-way radio, the walkie-talkie,
4 whether looking at police and fire, people like that
5 wouldn't be a more prevalent population of workers
6 using them.

7 DR. MOULDER: They are mostly going to
8 body-worn now with the microphones up here.

9 DR. LOTZ: Yes, that is common and Q. may
10 know more about the use, but there a lot of security
11 people -- I think there has been kind of an expansion
12 of use of the two-way.

13 DR. MOULDER: And those are three to five
14 watts?

15 DR. BALZANO: It depends on the frequency
16 band. There are two watts and as high as five, six
17 watts at 150 megahertz. There has been a certain
18 amount of usage of what they call the shoulder
19 microphone, but is still a small percentage.

20 You see them -- a policeman on a motor
21 bike that use that. But otherwise, for policemen or
22 firemen, they use the traditional push to talk in front
23 of the face. Exposure is different because exposure is
24 controlled as far as that, so you are looking for eyes
25 and frontal lobe. That is certainly exposure to look

1 at.

2 DR. McBRIDE: What about band width
3 differences?

4 DR. BALZANO: What do you mean by that?
5 Just band width? Band widths are much narrower except
6 for some of the military can be wider, but if you are
7 looking at policemen and firemen, emergency is a narrow
8 band on radios.

9 DR. LOTZ: I think one of the problems
10 with them potentially is because it's only an exposure
11 during push-to-talk, that there really aren't a lot of
12 minutes of exposure there for most cases. Even though
13 they carry them all the time, it's not like a cell
14 phone and if you have got it all the time, it's doing
15 something.

16 So, that reduces the exposure greatly.

17 DR. BALZANO: Those are called dispatch
18 for exactly that reason. Some of them may have what
19 you call inter-connect. You can use it as a phone, but
20 most of them are just -- they are rated 5-5-90 -- 90
21 percent of the time they are receiving, five percent of
22 the time, it's transmitting and five percent of the

23 time, is receiving. Some of them are 10-10-80, but
24 generally except in some situations like surveillance,
25 which there may be more transmission --

1 DR. MOULDER: Should be the actual minutes
2 of transmission are pretty low.

3 DR. BALZANO: Most cases are eight to 10
4 minutes a day, as much as half an hour. In some cases,
5 some maintenance personnel -- but again, if they use it
6 in their fashion, even if they use it three to five
7 watts, because of the distance, you get more exposure
8 in picking up the device and putting it against your
9 body because of the distance. It makes a big
10 difference. The power goes up with the square of the
11 distance. It goes from zero to -- there is a big issue
12 there.

13 Someone said about exposure of the brain.
14 Turns out that in most cases, the brain is not the most
15 exposed organ. So, yes, there is exposure of the
16 brain. It can be measured, but the biggest exposure is
17 not necessarily the brain.

18 DR. McBRIDE: So, we are suggesting there
19 really aren't any occupational groups that you could
20 easily follow.

21 DR. INSKIP: One group that was mentioned
22 was -- Bob Cleveland mentioned that there are a fair

23 number of people who work as service men on TV/radio
24 broadcast towers and potentially are really highly
25 exposed. I mean, they actually experience burns due to

1 exposure, but I don't know how one would go about
2 assembling a cohort.

3 DR. MOULDER: They may be unionized and
4 might we not -- a small number of them and I think
5 there are mostly union, so it might not be impossible.
6 They are also concerned about it, so they might be
7 interested.

8 DR. LOTZ: It's not going to be easy. I
9 am not sure, Peter, if we are talking about the same
10 group, but we have been trying to get in touch with
11 tower climbers and that would be more general. I mean,
12 they are probably doing the most with cell phone towers
13 themselves, because there are so many new ones.

14 But actually, there are a lot of
15 independent people out there, non-unionized. They make
16 a lot of money at it. They know it's a risky business
17 -- mainly from risk of falls, not risk of exposure and
18 they -- I don't know what is the right phrase, but sort
19 of in the US, it's sort of a cowboy attitude of it's a
20 tough life, but I make a lot of money and I will do
21 while I can, do I am not -- they definitely have the
22 potential of being a highly exposed group, but I think

23 it would be hard to assemble a cohort.

24 DR. INSKIP: What is your sense including

25 cell phone tower climbers? What total number in the

1 country would you talking about? Tens of thousands?

2 DR. LOTZ: We have been having a hard time
3 putting a number to it. I think many thousands and
4 probably a few tens of thousands, but -- and that is
5 probably increasing. NIOSH has actually gotten
6 involved with trying to follow it more from a fall
7 standard, standpoint because there have been around a
8 hundred deaths in the last five years or so from falls
9 on towers.

10 DR. BALZANO: They don't use the safety
11 equipment?

12 DR. LOTZ: Oh, yes, they know it. Well,
13 you have two things. One, you have, because of the
14 rate of new towers being put up, you have people
15 getting into the business who don't take time to do it
16 right. Then there are all kinds of other situations
17 where the hoist equipment isn't maintained properly and
18 it fails and drops them essentially. Or once in a
19 while, something is not -- in the course of
20 construction something is not put together right and
21 then the tower itself fails.

22 Then sometimes, a person falls and nobody

23 really knows why. They were presumably doing things
24 properly and they changed from a tie off from one
25 position to a tie off of another and slipped in

1 between. We have even wondered occasionally whether or
2 not a burn had something to do with it -- causing a let
3 go type of response. But usually in that case, you
4 don't have any way to find out.

5 DR. MOULDER: But if you are having
6 trouble in a cohort with something as straight-forward
7 as causing a death by falling, then our idea of trying
8 to use that for something like cancer would sound
9 pretty silly.

10 DR. LOTZ: I think it's a formidable
11 question.

12 DR. MOULDER: What about other military
13 exposures? Has that been done to death in the old
14 days? In the Korean War, they looked at radar
15 exposures -- totally different exposures. It could
16 still be going on.

17 DR. LOTZ: I don't know. Mary has
18 probably looked at those more than I have. I don't
19 think those studies are very strong.

20 DR. McBRIDE: General exposure assessments
21 are difficult because everything -- there are so many
22 different types of non-ionizing radiation exposure.
23 It's not that they used this sort of job exposure
24 matrix type approach to assessing characteristics of
25 exposure.

1 DR. MOULDER: The only other major
2 occupation source I know of is probably even worse and
3 that RF heat sealers and welders.

4 DR. McBRIDE: Yes.

5 DR. MOULDER: That is even worse exposure
6 assessment.

7 DR. LOTZ: Actually, you can identify the
8 cohort exposure assessment especially with some of the
9 newer technology. It can be very good.

10 DR. MOULDER: Okay.

11 DR. LOTZ: You have even got data logging,
12 light weight induced current meters and things like
13 that now. Barb has had experience at that. I think
14 still getting a sizeable group of them -- because they
15 are scattered around in small businesses generally.

16 DR. GRAJEWSKI: What is left and has not
17 been shipped out to other countries, right? We had
18 tremendous difficulty and this was back 10 years ago
19 when we did find water mattress operations clustered on
20 the east coast, but trying to assemble a similar female
21 cohort, I believe most of these operations have moved
22 out of the country.

23 DR. OWEN: Now is probably a good time to
24 break and start back in maybe 30 minutes.

25 (Off the record.)

1 DR. OWEN: I just told Ken that I was
2 going to put him on the spot. Since you weren't able
3 to be here right at the beginning, I thought we would
4 revisit a little bit of what we started with this
5 morning, and that was we started saying a few things
6 about the NCI study and the Muscat study and what kind
7 of things we got out of those and what data gaps there
8 were.

9 We discussed that only very briefly, so I
10 just wanted to give you a chance to add, even though
11 you didn't hear what was already said, to that.

12 Then I thought we could go on to you
13 talking briefly about your own studies and what kind of
14 data gaps there might be there. We jumped into that
15 somewhat as we did our discussions in terms of
16 planning, potential and cohort studies and so on.

17 And then another thing -- and this, of
18 course, is not all on you. I am just giving you a
19 chance to be the first one to talk. I would also like
20 people to volunteer what they know about ongoing or
21 just starting studies even though obviously we don't
22 have representatives of all the ongoing research. Just
23 whatever people do know about those studies, because
24 it's important for FDA to take into account what needs
25 are being addressed by ongoing studies, because when we

1 get to the point of needing to make recommendations to
2 CTIA, we want to be as nearly focused as possible and
3 not make any wasteful recommendations, so to speak to
4 maximize our gain.

5 Then finally, we might not get back to all
6 this before we break for lunch, but as I mentioned
7 earlier, we have got copies of excerpts from some
8 recent activities and recommendations and I wanted to
9 eventually draw attention to specific parts of those
10 recommendations and draw input in response to those
11 various recommendations from other groups.

12 DR. ROTHMAN: I am not sure what you
13 wanted me to start by adding to.

14 DR. OWEN: Well, since you weren't here
15 when we briefly discussed the case control studies that
16 were published in December and January, I just wanted
17 you to have an opportunity to give your view point on
18 what we got out of them and more importantly what the
19 data gaps are and what might be needed to work on the
20 studies to address those data gaps.

21 DR. ROTHMAN: Well, I will have only a
22 very brief comment on that. I think we know more than

23 we did with the publication of these studies and they
24 did provide some reassurance, but it was limited and it
25 said so in the actual reports. I mean, the authors I

1 think were fairly circumspect about the conclusions
2 that they drew and rightly so.

3 For one thing, the publication of any
4 epidemiologic study is the publication of the
5 historical exposure and exposures that were being
6 studied were in fact representing a technology that was
7 changing rapidly. So that was one limitation.

8 A more severe limitation is that average
9 length of time between the bulk of the exposure and the
10 events that were studied were short. So, these studies
11 were limited to providing reassurance about short
12 induction time carcinogenesis and they don't really
13 address long induction time carcinogenesis. So, that
14 is another limitation.

15 Then there are despite good attempts I
16 think to get accurate information, it persists a
17 question in any study that shows no effect, any
18 epidemiologic study, there is always a question about
19 whether or not exposure misclassification has obscured
20 an effect and that is a lingering question not just for
21 these studies, but virtually any study of a like issue.

22 So, these are the main limitations that we

23 have in terms of what we can get out of these studies,
24 but nevertheless to get back to what I started with, we
25 are better off having these studies than without. We

1 know more now and we do have this reassurance and that
2 is good.

3 It's probably not enough I think to settle
4 the issue in the minds of the public and possibly not
5 for regulatory agencies, but it certainly is a start.

6 DR. OWEN: So, since I am revisiting that
7 that topic, does that bring to mind -- does anybody
8 else want to add to that before I try and move us to a
9 different topic? Okay.

10 So, as I said, even though we jumped into
11 talking about a lot of the kind of cohort studies that
12 can be done, maybe you want to recap your own work and
13 at least your own viewpoint on what limits there may
14 have been or what data gaps exist.

15 DR. ROTHMAN: Do you want to talk about
16 the cohort study that we did?

17 DR. OWEN: Yes.

18 DR. ROTHMAN: That was a study that was
19 conceived with a plan to do a very large study with a
20 relatively short follow-up and the size was intended to
21 compensate for the short induction time, because if you
22 imagine that there is a long induction time effect,

23 typically there is variation in induction times which
24 is enough so it will be a gradual upswing in terms of
25 cancer occurrence that would start many years before

1 the peak would be reached.

2 So, even if there is a 20 years peak,
3 there might be an upswing that might start among a
4 small number of cases even three, four, five years out
5 from the beginning of exposure. So, the idea is that
6 if you had a big enough study, you might even begin to
7 detect that.

8 So, the plan was to do something based on
9 a large number of people and to get rapid results.
10 This was undertaken back in the early to mid 90s when
11 there was little information and plenty of public
12 concern.

13 To do this, given the large numbers and of
14 course limited budget as is often the case, we did a
15 completely record-based study where people were
16 enrolled based on information that was collected by
17 carriers. And then our attempt was to link this
18 information directly to information in the national
19 death index and to use mortality as a surrogate for
20 incidence. That is mortality was the end point.

21 So, I think the plan was a good one and it
22 would have worked very well if we hadn't gotten bogged
23 down with one simple little problem which was a lawsuit
24 that was filed by a plaintiff's attorney in Chicago
25 that put a halt to the entire project right in the

1 middle.

2 The project really never recovered from
3 that lawsuit. In fact, the lawsuit continues to this
4 day. I am not following it actively, but I know it is
5 continuing to move along and has had a much longer life
6 than the study itself unfortunately.

7 So, what we ended up with was very limited
8 follow-up information on only a portion of the cohort
9 rather than on the entire cohort that we had intended,
10 so we ended up with insufficient information really to
11 draw any good conclusion about brain cancer, which was
12 the main focus of the study.

13 We did end up with enough information to
14 quantify what we think is the biggest effect of using
15 cellular telephones, which is the mortality rate from
16 motor vehicle accidents. So, even though that wasn't
17 the intended object or main object of the study, it was
18 -- the study even in the more limited form that we had
19 was big enough to find a substantial increase in the
20 risk of death from motor vehicle accidents and that was
21 reported in the Journal of the American Medical
22 Association last November.

23 DR. OWEN: You had a question?

24 DR. LUNDQUIST: I want to make a comment
25 about that lawsuit. I feel that lawsuit from the

1 scientific perspective was extremely unfortunate and
2 this is in my view one of the reasons why it is
3 imperative for the agencies of the federal government
4 to do these studies.

5 DR. OWEN: I know you weren't able to be
6 here at the beginning of the meeting, but actually
7 earlier today, I pointed out that I thought that
8 discussion of the lawsuit really didn't have a part in
9 this meeting because it has to do with the logistics of
10 conducting studies and it is something that FDA has to
11 worry about, but it's not part of collecting the
12 scientific input that we are trying to collect.

13 DR. LUNDQUIST: I agree, but when you have
14 these legal bars to one party doing a study and these
15 legal bars do not exist for another party doing the
16 study, then it begins to be important who does the
17 study.

18 DR. OWEN: I realize that.

19 DR. LUNDQUIST: And I just thought I would
20 call people's attention to that.

21 DR. OWEN: Thank you. As I said, I was
22 interested in having people volunteer what they may
23 know of ongoing studies or recently planned studies. A
24 couple times people have referred to the IARC studies
25 and actually I was wondering if maybe you, Q., could

1 start off with telling us a little bit more about that
2 dose phone aspect of that study.

3 DR. BALZANO: Yes, one of the steps at the
4 beginning of the study has been to distribute a certain
5 number of phones in various part of Europe to determine
6 pattern of usage and exposure level.

7 The phones are instrumented. They look
8 like a normal phone. It's just a little bit thicker
9 because we have to go in with additional printed
10 circuit board, but it will giving you following
11 information, laterality -- whether it is being used on
12 the left or the right. It will tell you periodically
13 what is a level emitted by the phone, so you have an
14 idea. And of course, it measures the time, the
15 duration during the day of the phone call and also an
16 important point, is the fact that it gives you an idea
17 of the tilt of the phone -- both this way and that way.
18 That would help in establishing on a statistical basis
19 again -- this is strictly for statistical purposes --
20 which part of the head.

21 DR. MOULDER: Did you also say that it
22 could monitor how far the phone was away?

23 DR. BALZANO: Yes, there is a monitoring
24 system there that tells them that, because at that
25 point, you shift the exposure. In this condition, the

1 exposure is going in this area and if you tilt it
2 substantially enough, the exposure shifts.

3 As far as I know, the data is being
4 collected, but I haven't received any yet.

5 So, the phones were distributed a while
6 back -- about three or four months ago and by now, of
7 course, the data is being collected. Since I retired,
8 I kind of lost contact with Elizabeth Cardis, so since
9 then, as far as I know there are about 100 phones that
10 have been distributed. And as far as I know, they were
11 taking them around Europe to get an idea of what are
12 the exposure patterns in the various countries because
13 country by country, there might be difference in
14 installation and also the way the people use them.

15 The US should be more homogeneous --
16 might. We will find out whether that is true. So,
17 that is as far as I know.

18 DR. OWEN: What about -- what do we know
19 or what does anyone know that appears to be missing in
20 the study designs of the IARC studies that we might
21 want to keep in mind, not only in the exposure
22 assessment aspects, but other aspects of study design?

23 I am not sure who, if anyone here --

24 DR. LOTZ: Joe is involved in the exposure

25 assessment.

1 DR. OWEN: Joe --

2 DR. LOTZ: So I know a little bit indirect
3 from talking to him and I think at least their initial
4 questionnaire instrument was very extensive, designed
5 to try and identify occupational exposures from other
6 electromagnetic sources and things like that, but I
7 don't know the details.

8 DR. MOULDER: I saw a copy of their
9 meeting in London and they are asking people about
10 model of phone used, estimated number of minutes of
11 phone use, how they used it. I agree -- it went on for
12 pages.

13 DR. McBRIDE: The Canadian group, we are
14 going to be part of the IARC study. We are the last
15 country to get started actually. And that will be
16 based in Vancouver, Ottawa, Montreal centers. One
17 thing we were concerned about was the plan to collect
18 information on other occupational exposures was
19 somewhat limited, so we have added a component, another
20 CADI questionnaire that looks at occupational
21 exposures, other occupational exposures to brain
22 cancer, in particular using a job exposure matrix that

23 Jack Simiticky (phonetic), who is one of our co-
24 investigators, has developed and used extensively in
25 hospital settings among another situations.

1 So, we are hoping to add something for our
2 component.

3 DR. LOTZ: Mary, you are saying that you
4 are adding not electromagnetic sources, but other
5 things of interest.

6 DR. McBRIDE: Other things for the most
7 part, yes.

8 DR. OWEN: IARC stands for the
9 International Agency for Research on Cancer, by the
10 way.

11 Thanks. That's very helpful to know.

12 DR. RINSKY: Sort of a generic comment
13 about large studies of this kind, especially when they
14 go across country, so there is a attempt to always
15 increase the size of the cohort for the purpose of
16 increasing precision. I think that there is a real
17 danger of getting a very precise estimate around --
18 getting very precise about a biased estimate.

19 The problem being that the combinations
20 that these different countries bring into the extreme
21 heterogeneity between not just their exposures, but
22 their cultures and their genetic pool and everything

23 else that is involved.

24 These really aren't pooled studies in that
25 they are going to be reported on separately and then go

1 through a meta analysis rather than a comparison and a
2 pooled fashion, so I don't see how it's possible for
3 anything but the largest risk to get through this
4 curtain of heterogeneity and we already that there is
5 not a large risk involved here or we would have seen it
6 in the other efforts that have been done.

7 So, what is going to happen in the end is
8 this grand announcement of a several hundred thousand
9 member cohort which is equivocal when looked at
10 separately and when pooled is going to be negative.

11 I don't think it's particularly helpful.

12 DR. ROTHMAN: Are you speaking of the IARC
13 study?

14 DR. RINSKY: Yes, I am.

15 DR. ROTHMAN: Isn't that a case control
16 study?

17 DR. RINSKY: Yes, it's a case control
18 study that involves a lot of different populations and
19 a control for a particular case cannot come from any
20 other country. It's going to be -- the control is
21 going to be matched by population to the case. It's
22 not really pooled. It's more a combination of odds

23 from the different places.

24 The other thing is that while the -- at

25 first blush it appears to be very comprehensive of

1 large questionnaires that seem to touch on every
2 particular detail, these are being applied by very
3 different groups. And they are not always applied --
4 they are never applied equally because the logistics
5 are different for each group that is supplying the
6 list.

7 DR. McBRIDE: Both those issues certainly
8 have been addressed by the overall group. The issue of
9 a biased estimate has a lot to do with for example your
10 sources of population controls and your source of
11 cases, too, in some cases.

12 DR. RINSKY: Right.

13 DR. McBRIDE: And one of the criterion in
14 the protocol is that in general they were looking for
15 investigators that could and had demonstrated to have
16 provided in the past, access to case groups and
17 controls groups that were as much as possible
18 population based rather than institution based.

19 The second issue -- I have lost it.

20 DR. OWEN: The different application of
21 the instrument?

22 DR. McBRIDE: Yes, the application of
23 instrument. I mean, that is a problem with any multi-
24 sensor study even within a country and I know there are
25 several processes that have been put in place for

1 training and also ongoing quality management. Now, you
2 can argue one way or the other how appropriate those
3 are and in the end, you are right, you are not going to
4 eliminate heterogeneity.

5 You need to do more of a meta analysis
6 than actually pool the data, but the question is will
7 this in the end give you more information or better
8 information than you had from the individual studies
9 before alone and certainly, the size of the group you
10 need -- the thought was even with those problems, that
11 it will.

12 Now, the big limitation is it's only
13 looking at certain outcomes and yes, we will get more
14 information on sub-types of brain tumors and more
15 information on rare tumors like the tumors of the
16 salivary glands, but those -- there is a limited set of
17 cancer outcomes that one gathers.

18 DR. MOULDER: On the plus side, this will
19 have somewhat longer follow-up times than the earlier
20 studies just because historically they are done later,
21 so there may be some patients with narrow -- maybe even
22 10-year follow-up?

23 DR. McBRIDE: That's true.

24 DR. MOULDER: As opposed to the current
25 generation of studies which at best go back five to

1 seven years.

2 DR. LOTZ: Since it's a later study, I
3 would presume that to be the case, John, but, the
4 Danish study is one where at first glance it looked
5 like they had a long time, but it turned out to be a
6 very small percentage of users that actually had
7 substantial time. I forget, but it was something like
8 two-thirds of them were less than five years and half
9 were less than two years.

10 DR. MOULDER: As I recall, that study was
11 actually done starting in '97, so I am thinking these
12 are studies that are being done starting in 2000, 2001,
13 so I hope we are going to add three or four years to
14 that?

15 DR. LOTZ: Yes.

16 DR. MOULDER: Yes, it's still not going to
17 be large numbers of people over 10 years for follow-up
18 clearly, but it's going to be a few more years than the
19 current generation.

20 DR. LOTZ: Right.

21 DR. BALZANO: Exposure was up to 1989. Up
22 to 1989, there was restricted use. There was still a
23 restricted number of people.

24 From 1989 to 1992, 1993, that is when you
25 really start getting your growth, so that is where you

1 really started getting your population.

2 Dr. Cardis and Professor (inaudible) were
3 very sensitive to the issue, so they were really trying
4 to pull down some quality criteria on administering of
5 the various questionnaires. They were very, very
6 sensitive to it and I think that they went extensive --
7 they were trying to cross-correlate the outcomes. So,
8 I think that, yes, your concerns are correct, but I
9 think that by design they are trying to bring the best
10 possible --

11 DR. RINSKY: I agree they are extremely
12 sensitive to it, but that doesn't mean they can
13 surmount and insurmountable problem.

14 DR. BALZANO: They can try to minimize it.

15 DR. MOULDER: Where are these studies --
16 how many years from now are there likely to be results
17 starting to be publicly available for these?

18 DR. McBRIDE: Four or five years.

19 DR. ROTHMAN: Have any of them actually
20 begun, Mary?

21 DR. McBRIDE: All the studies -- all the
22 countries and I think there are 13 countries -- 12
23 countries and 13 investigators --

24 DR. RINSKY: What is the real chance that
25 13 countries are going to call glioblastoma the same

1 thing? Even with diagnosis, it's not going to be the
2 same.

3 DR. McBRIDE: There is in the protocol --

4 DR. RINSKY: There are language problems -
5 -

6 DR. McBRIDE: I mean, these are problems
7 that are there for any epidemiologist.

8 DR. MOULDER: Most epidemiology studies
9 don't go cross country.

10 DR. RINSKY: Yes, as far as I know, most
11 epidemiologic studies work very hard to reduce this
12 sort of thing -- not to the opposite, which is the
13 maximize numbers at the sacrificing of --

14 DR. McBRIDE: I don't know how available
15 the protocol is. In terms of diagnosis to get
16 consistency and validity of diagnosis -- for example,
17 the protocol requires that certain tests be done, that
18 reports be collected and those be submitted, along with
19 slides and a central review.

20 DR. RINSKY: So, every non-case is going
21 to have all it's slides reviewed to make sure it's a
22 non-case? Obviously that can't happen.

23 DR. McBRIDE: No.

24 DR. RINSKY: There are some major
25 deficiencies to the concept of a pooled study and I

1 don't care -- all the sensitivity in world isn't going
2 to overcome that.

3 DR. McBRIDE: No, there are not too many
4 brain cancers --

5 DR. RINSKY: I don't know that. In all 13
6 countries that is the case?

7 DR. McBRIDE: Twelve.

8 DR. RINSKY: Thirteen countries --

9 DR. McBRIDE: This is not my study.

10 DR. RINSKY: Can anybody tell us what the
11 13 countries are?

12 DR. INSKIP: Nine in Europe, I think, and
13 Israel, Australia and New Zealand, Canada.

14 DR. ROTHMAN: I think the international
15 aspect is certainly an issue one would be concern
16 about, understanding the study. But still for me, the
17 big problem will be -- let's imagine for sake of
18 discuss that if you use a cell phone actively for 10
19 years, it doubles your risk of some brain cancer and
20 let's imagine in this study that is going to be
21 conducted, that only let's say five percent of the
22 people will have used a cell phone for 10 years. So
23 that means that you are going to have one extra case of
24 brain cancer for every one that would have occurred in
25 five percent of the people and in 95 percent of the

1 people, you won't have any change.

2 So, that means that instead of 20 cases of
3 brain cancer, you will have 21. Now, that means that
4 theoretically -- I mean the study should be able to
5 pick that up. It was designed to be able to pick up
6 something like that if it is done very well. It's not
7 going to be able to suffer much deviation from what is
8 needed in order to protect that kind of effect.

9 If you contrast that with doing a cohort
10 study, especially a prospective cohort study, and now
11 you are comparing the heavy users with light users or
12 non-users and now you have a contrast that makes it
13 much easier to pick up a doubling of risk.

14 So, a case control study is really not the
15 best approach to try to find an effect like that, so
16 one of the handicaps that this study faces is that it
17 just by design is not going to be able to do it.

18 So, one of the handicaps that this study
19 faces is that it just by design is not going to be easy
20 to do, to find that kind of effect which would still be
21 of great interest.

22 DR. RINSKY: To switch subjects, the only
23 other thing that I wanted to comment on with regard to
24 the dosimetry, to the presumed radio-sensitive parts of
25 the head, while it's probably reasonable to think of

1 the mechanics of this disease process if it's real as
2 being dose-related to a particular exposure to a
3 particular part of the head, I would remind people that
4 if you hit the retina with ionizing radiation, you get
5 sarcomas of the long bone in the leg. The fact is we
6 really don't know the mechanism of a disease we really
7 don't know exists.

8 It could just as easily be some
9 biochemical communication between one cell and another
10 cell as it is exposure to a particular area of the
11 brain. So, I would caution about getting married to
12 the concept that if you switch exposure from upper part
13 of the head and lower part of the head, that you have
14 necessarily made any difference in risk, although it
15 may turn out that you have. Just don't get yourself
16 convinced of that ahead of time.

17 DR. MOULDER: That is where the history of
18 people like Mary who worked on the Pomeroy thing come
19 in. If there is a risk, you have no idea what the
20 correct dose metric is.

21 DR. RINSKY: That is what I was trying to
22 say and I couldn't get it out.

23 DR. MOULDER: This is a problem actually
24 with available dose metrics, probably even worse in the
25 power line case. The only way to get around that is

1 you collect everything in sight and then worry about
2 multiple comparisons later. Neither biophysics nor the
3 animal studies give you any suggestion of where to go
4 for dose metric.

5 DR. McBRIDE: I guess that is the point I
6 would make, too. I mean, it's one thing to look at the
7 studies that have been recently published and find out
8 where there is a positive finding in a sub-group here
9 or there, but one would like to use the laboratory
10 studies to inform the epidemiology as to what metric or
11 as to what outcomes we should expect. It's not helpful
12 in this situation.

13 DR. BALZANO: If I heard you correctly,
14 then what you are saying is you don't have to look only
15 at the pathology of the brain. You at pathologies, if
16 I heard you correct.

17 DR. RINSKY: Right, but I think the point
18 is I don't know what the right metric is. As far as I
19 know, duration is just as important as location or
20 something --

21 DR. BALZANO: Location, duration and
22 intensity. You put those three together, you should be
23 able to make some sense out of it.

24 DR. MOULDER: But you have people out
25 there saying that digital versus analog might make a

1 difference. You have a few people claiming that even
2 the type of analog might make a different.

3 DR. McBRIDE: If you postulate a threshold
4 effect rather than a response --

5 DR. BALZANO: The point is, if you know
6 the intensity, you know the duration and you know the
7 location, you can reconstruct all of the above.

8 DR. MOULDER: In a cohort study.

9 DR. BALZANO: Yes.

10 DR. MOULDER: With a cohort study though,
11 you don't have to pick your end points in advance, do
12 you?

13 DR. ROTHMAN: No, not end points.

14 DR. BALZANO: No, at this point, I think
15 that the case control is not going to help very without
16 going to a cohort first.

17 DR. MOULDER: If you had all the money in
18 the world to do a case control study in the United
19 States, could you do a better one -- especially if
20 somebody else got to do it -- could you design a better
21 one than the one IARC is doing now?

22 DR. ROTHMAN: I think the IARC design is
23 quite solid. I think the limitations are inherent to
24 the approach, not so much to the execution.

25 DR. OWEN: Thank you for asking the

1 question that way. I think that was very helpful.

2 DR. INSKIP: It seems absent real
3 compelling epidemiologic or experimental, theoretic,
4 whatever, we need to pursue in terms of metric at
5 point, because we don't know whether there is or is not
6 an effect -- just questions on the order of people who
7 use them more and use longer are at higher risk than
8 people who use them less, is still a pertinent focus.
9 And in terms of getting into all the issues that can
10 modify the level of exposure and might make a
11 difference in threshold, it would seem that if there is
12 really something there, if we can develop a means of
13 adequately separating the long term heavy users from
14 the non-users or short term users, if there is
15 something there, we should be able to detect it.

16 One might assume that even if it's not
17 cumulative use that is important, the relevant thing
18 that might be important is is there strong reason to
19 believe that that would be distributed or be in balance
20 of that in respect to a metric of cumulative use.

21 You can start out with a totally
22 pessimistic attitude that we can never hope to learn
23 and just measure everything, but I believe that if
24 there is something there, long term studies that can
25 get at heavy users versus light users should tell us

1 something.

2 I would be leery of doing too many
3 multiple metric analyses in the absence of some link
4 because I am not sure what that is going to tell us. I
5 think there is a strong risk of false positives by
6 doing every sort of metric one can conceivably think
7 about and that begets another X million -- so, I think
8 key option would be to separate long term users from
9 the lighter users.

10 DR. ROTHMAN: Peter, how do you weigh the
11 false positive cost against the false negative cost
12 without looking at various metrics in case there is one
13 metric that is better than --

14 DR. INSKIP: I think in a case control
15 setting, when there is marginal cost to collect
16 additional information, you do collect that. But in
17 the absence of a strong overall effect of duration,
18 level of use, some appropriate metric with an allowance
19 reduction period, if that over result is negative, I
20 would be leery -- I would not push an interpretation
21 too far of the sub-group in a metric analysis.

22 DR. ROTHMAN: Well, they are not sub-
23 groups though -- not like a sub-groups analysis. It's
24 just a different categorization of exposure, a
25 different measurement of it for the entire population.

1 DR. INSKIP: It is, but I think one has to
2 have a strategy for what -- where one goes from there
3 once one has 20 different metrics and if there is no
4 thought or context, empirical, epidemiologic,
5 experimental in which to interpret that --

6 DR. ROTHMAN: Would you be happier if the
7 metrics were specified to correspond to certain
8 biological hypotheses perhaps before the analyses were
9 undertaken?

10 DR. INSKIP: That would be an improvement
11 over just a collection of any metric I could think of -
12 - related to some hypothetical mechanism, yes. The
13 idea of an international study inherently having
14 insurmountable obstacles -- that's an overly
15 pessimistic attitude to me. The idea of studies being
16 done in multiple countries -- they have made a strong
17 effort, I believe, to standardize the instrument for
18 that purpose. So at least in principle, the instrument
19 has been standardized. You are absolutely right, but
20 it's not enough to develop a protocol and instrument.
21 You have to implement it effectively and it's incumbent
22 upon the IARC managers and investigators to do that.

23 But, as was pointed out earlier, many
24 epidemiologic studies are multi-center studies whether
25 it be North America or Europe. And when one does

1 multi-center studies with a view towards pooling
2 results later, certainly one looks for heterogeneity
3 across centers as part of that analysis.

4 But to assume that there is going to be
5 heterogeneity that one cannot make sense of a priori I
6 think is defeatist. I think Ken made a good point,
7 that when you are up to a potentially small number of
8 excess cases, then even small deviations are important
9 and can cause you to miss something you might not
10 otherwise see, but if you are going to get large
11 numbers of cases, that oftentimes -- brain cancer is
12 not a common disease.

13 It's not easy to put together a cohort to
14 get real large numbers of cases, so I think a case
15 control approach at this point has advantages. I think
16 the IARC study was well-designed within their
17 capability. Perhaps the relative risk for heavy users
18 isn't two. Maybe it's four. I think it's important to
19 look.

20 If one is going to make the objection that
21 we cannot do multi-center studies because of
22 heterogeneity, there are going to be many -- like never

23 study childhood cancer --

24 DR. RINSKY: Actually I didn't say

25 anything about multi-center studies. I said this

1 particular international study. And it might be
2 colored by my experience with IARC because I was on
3 their board for their international radiation studies
4 and I see how in practice these studies -- the theory
5 is fine, the protocol is fine, in practice, it don't
6 work. Different countries simply have different
7 constraints and they can or cannot adhere to the
8 prescribed protocol, which is extremely sensitive to
9 the problems of heterogeneity. It doesn't work.

10 So, beyond defeatist --

11 DR. INSKIP: Heterogeneity with respect to
12 what? The way the study is carried out? The basic
13 population --

14 DR. RINSKY: If you have 13 countries
15 working on something, then you have at least 13
16 different study teams. I don't know about you all, but
17 when I am dealing with a multi-center site that has
18 three different study teams and we are all from
19 basically the same culture and we can't get people to
20 work the same, ask the same questions the same way, I
21 don't know how there can be any reasonable expectation
22 at all that you are going to collect this data the same
23 way. And it seems to be then that the answer to the
24 pooled analysis, which I repeat is not a pooled
25 analysis -- it's a combined analysis. The odds ratio

1 is combined -- a person cannot serve as a control for a
2 different case from another country.

3 So, it's preordained that the combined
4 analysis is going to -- because I believe that there is
5 a very small risk, if any -- it's going to be negative.
6 And then when they do the country-specific ones, some
7 will be positive, some will be negative. You don't
8 have to do the study. We know the outcome.

9 DR. INSKIP: What is the distinction you
10 are saying -- it's not a pooled analysis, it's a
11 combined analysis? If I do a study at three hospitals
12 in the United States and I match on age, sex, race and
13 hospital, that is the same as matching on age, sex,
14 race and country. It's still -- it's one more matching
15 criteria in your study.

16 DR. RINSKY: I could go into this, but I
17 am not sure it's relevant.

18 DR. INSKIP: Okay.

19 DR. RINSKY: There are ways to do -- and
20 there are people around this table who have much
21 greater expertise than I do in this, but there are ways
22 that one can say here is your exposure, here is your
23 disease experience, now let's contrast that with
24 someone else with an opposite disease experience
25 regardless of what country you are from. That is what

1 I would consider pooled analysis. That is not how this
2 thing is designed.

3 DR. ROTHMAN: That is the way
4 epidemiologists use the phrase. They distinguish a
5 meta analysis from a pooled analysis mainly by the
6 criterion of whether or not you can actually use the
7 data altogether in a single analysis.

8 I think what Peter is saying is that you
9 can have data that is pooled in a single analysis that
10 come from different places, whether they be hospitals
11 or countries, and it doesn't really argue -- at least
12 not in the terminology that we use that it's not a
13 pooled analysis.

14 A meta analysis, you don't have individual
15 level data for a single people. You have instead just
16 data that in the aggregate describe what happened in
17 the various studies or groups. And then you have to
18 combine that just by averaging the results.

19 So, may be is in part a terminology issue,
20 but I think that what they are planning is what
21 epidemiologists would call pooled analysis. They are
22 going to take the data from each center and then
23 analyzed it perhaps separately in addition, which is
24 often what happens in a collaborative study, but then
25 also in a single overall analysis.

1 DR. RINSKY: I guess I would have thought
2 of something that is done in from separate centers and
3 then combined as a very well done meta analysis.
4 Whereas, if it was considered as all one risk set, that
5 is how I would have defined pooled, so we have a little
6 terminology difference.

7 Fundamentally though, I don't think there
8 is any reasonable expectation that large instruments
9 can be really applied -- again, different cultures,
10 different languages and that sort of thing -- and still
11 allow a subtle problem to peek through the noise, the
12 din of all the mis-classification.

13 I don't want to beat the horse to death.
14 It's something to consider and I would only warn
15 against this be considered the definitive study,
16 because you are going to -- I think there is a good
17 chance you are going to end up with a false negative
18 and because of the size and the effort and the money
19 and everything else that goes into it, it's going to be
20 billed as and accepted as the definitive study.

21 DR. MOULDER: I don't really think that is
22 the critical question I have here. Rather, it's given
23 what IARC is doing, is there any way that a US based
24 case control study could be any better?

25 DR. RINSKY: I --

1 DR. MOULDER: With all the problems of the
2 IARC study, doing our own is not going to improve
3 things any.

4 DR. RINSKY: I wouldn't argue with that.

5 DR. MOULDER: IARC is about as well as can
6 be done right now in case control.

7 DR. RINSKY: That may very well be the
8 case.

9 DR. ROTHMAN: And they had more exposure
10 longer in the countries where they are going to be
11 doing the study.

12 DR. BALZANO: That's is why, the case
13 control study doesn't make too much sense.

14 DR. ROTHMAN: And especially given that
15 IARC is conducting this particular study. To add
16 another one to it, I think that might be the Muscat
17 study.

18 DR. MOULDER: I agree with you. While
19 this may be called by some people definitive, it's not
20 going to be definitive pretty much no matter what its
21 outcome is going to be. The best it can do, if none of
22 the problems you are worried about happen, is tell you
23 that there is not a big risk in medium term use, which
24 is not answering all the questions the public has.

25 DR. ROTHMAN: And only for the sites, the

1 outcomes that they choose to pool.

2 DR. MOULDER: One of our purposes here is
3 to try and see what could be done with the resources
4 available in the United States which is not already
5 being done somewhere or where we could conceivably do
6 it better and the answer in the case control study is
7 that there maybe problems with the IARC study, but
8 there is nothing -- if we design our own from scratch,
9 it wouldn't be any better. It might just be different.
10 And it might not even be as good because the use in
11 this country isn't as long.

12 DR. RINSKY: As a case control study.

13 DR. MOULDER: Yes.

14 DR. RINSKY: But we are not saying that
15 about the cohort study that would be redesigned here.

16 DR. MOULDER: Speaking to whether there is
17 any point in trying to see whether there should be a US
18 case control study at the moment and I don't see any of
19 you saying that there are problems with what IARC is
20 doing, but we can't solve them. We can't do any
21 better. We will just get different problems.

22 DR. OWEN: The only thing that I recall
23 hearing earlier in the discussion is that there is
24 apparently less variability because it would not be the

1 cross-cultural difference if you had a study of equal
2 size here.

3 DR. MOULDER: We would not have as much
4 exposure duration.

5 DR. OWEN: Right.

6 DR. McBRIDE: One of the issues is whether
7 or not a case control study looking at another outcome
8 would be useful.

9 DR. LOTZ: Mary, how similar is the use
10 pattern in Canada to the US?

11 DR. McBRIDE: I don't know enough about
12 the use pattern here, but certainly there was not a
13 great deal of use until the later 80s, early 90s just
14 as you are saying. So, I think it is quite similar,
15 but certainly behind Europe.

16 The one difference I would say is that
17 there are fewer companies operating in Canada. People
18 don't switch from company to company as much.

19 I just wanted to say a little bit more on
20 the issue of outcome. I guess one can read the
21 theoretical possibility that we should be looking at
22 some other outcome, either another cancer outcome or

23 another health condition and I say health condition
24 rather than biological effect, but there are things you
25 can measure. I guess I would add to that that there is

1 probably not enough evidence to suggest another likely
2 outcome sufficient to build a case control study
3 around, which is another argument for a cohort study.

4 Certainly, one can be informed about the
5 types of outcomes one would look at in a cohort study
6 by whatever evidence is out there just as you would use
7 that to form your choice of metrics and there is a
8 difficulty, of course, in collecting good data on some
9 of the cancers -- sometimes you can use registries --

10 DR. MOULDER: Based on the public meetings
11 I have been to on this, which is large numbers of them,
12 number two after brain cancer is headaches and after
13 that comes a bewildering variety of other symptoms,
14 which I don't think can even be defined. So, if you
15 think that what you look for should be based on what
16 people are worried about at the moment, it's really
17 brain cancers, headaches and after that there are a lot
18 of people worried about things, but no two of them seem
19 to be worried about the same thing.

20 DR. McBRIDE: I guess I am suggesting we
21 don't use that criteria of what people are worried
22 about to inform outcomes.

23 DR. MOULDER: That's is why we are
24 studying brain cancers.

25 DR. BALZANO: There is proximity there.

1 DR. McBRIDE: Yes, the proximity of
2 exposure --

3 DR. MOULDER: Or you could use that as an
4 argument that headaches might be relevant.

5 DR. OWEN: Another one from this list is
6 leukemia, which some people will argue that that is
7 also the exposed tissue, why you are choosing that, but
8 --

9 DR. BALZANO: The question with the
10 headache though --

11 DR. MOULDER: I wasn't suggesting that
12 that be the subject of the case control study.

13 DR. BALZANO: If you want a new one, there
14 has been a very interesting study out of Switzerland
15 that came out about the effect on sleep. People that
16 use the phone towards the end of the day, have a
17 different sleeping pattern. Again, better to look into
18 pathologies.

19 DR. ROTHMAN: If I were studying headache,
20 I would be interested in knowing what people were
21 actually saying on the phone.

22 DR. BALZANO: That's right.

23 DR. MOULDER: I can't think of any biology
24 which pushes you to any other obvious end points to
25 assess.

1 DR. McBRIDE: In the Canadian report they
2 talked about -- and this wasn't my area of expertise --
3 looked at the possibility of EEG changes. That was
4 hypothesized. I am not saying that -- and there is a
5 change in some measurable health issues, but there
6 really wasn't too much that was defined. Alzheimer's
7 disease, degenerative diseases of the brain were
8 suggested also as outcomes. But there wasn't much.

9 DR. INSKIP: Did you mention ALS?

10 DR. McBRIDE: Sorry, I didn't, but ALS,
11 yes, was in there.

12 DR. LOTZ: Russ, that poses a question, I
13 guess, are we considering in this discussion non-cancer
14 end points?

15 DR. OWEN: Well, if I was only allowed a
16 one word answer, I would say yes, but I can say as much
17 as I want. I guess one thing to keep in mind, and I
18 tried to give a hint of this at the beginning, is that
19 what we are doing here right now is part of only one
20 facet of many things that are going on, but this
21 activity is part of the cooperative research agreement
22 between FDA and CTIA and its initial focus and main
23 focus was to follow up on what they had done earlier
24 and therefore, that would be following up on cancer
25 work.

1 Aside from that, I would also say that at
2 least with my sense within the FDA, is that right now,
3 still the main interest would be on cancer end points
4 rather than non-cancer end points. But at the same
5 time, if there were compelling hypotheses or data that
6 fell out of cohort studies that suggested other end
7 points, that they would certainly be fair game.

8 DR. McBRIDE: I guess I would suggest that
9 if one was going to collect data prospectively, it
10 might be a small add-on.

11 DR. BALZANO: We are in the same box
12 (inaudible).

13 DR. MOULDER: I didn't hear you.

14 DR. BALZANO: Ultimately, this is a
15 meeting where we are in the same box -- we are doing
16 the same thing, find out where this thing is landing
17 and without any preconceived opinions.

18 DR. INSKIP: Would you guesstimate that
19 the sort of web based cohort study of volunteers
20 comprised with six months recontact over 20 years,
21 would you say maybe an order of magnitude of lower
22 cost, sort of more traditional -- I am just getting at
23 the sample size issue, dollar issue for cohort studies.

24 DR. ROTHMAN: I think that would be a
25 target and it's not an unreasonable target just because

1 the huge logistics of the old-fashioned cohort studies
2 that continue to follow people over a long period of
3 time that involve mailings, codings, all sorts of work
4 aside from analysis, which is eventually going to take
5 up a lot of time. But the data collection effort is a
6 massive effort and I think that could be cut by an
7 order of magnitude.

8 Analyses would not be any better, but they
9 would be costs that would be faced at the end of the 20
10 years or well down the road and, of course, they could
11 be discounted.

12 DR. INSKIP: Sort of a second question I
13 had was whether --

14 DR. MOULDER: I don't understand. In this
15 dreamed up study, do you need a fixed amount of time to
16 do the analysis or do you analyze periodically as you
17 go along?

18 DR. ROTHMAN: You would analyze for motor
19 vehicle end points after a couple of years, but if you
20 are going to look at brain cancer, there isn't much
21 point in starting to monitor it if you are doing
22 surveillance. You would wait a while and then you
23 would start to look at it after a certain period of
24 time has passed.

25 DR. MOULDER: The way you answered his

1 question implies to me you would go for X numbers of
2 years and then do all the analyses and that is not --

3 DR. ROTHMAN: No, no, it's just that the
4 analyses get to be more heavily weighted toward the end
5 when you had lots of data rather than at the beginning
6 when you are collecting.

7 DR. MOULDER: Sorry, Peter.

8 DR. INSKIP: Well, I'm just -- because I
9 think what the incidence for brain cancer in the United
10 States over the range of adult ages is on the order of
11 17 per 100,000 per year or something in that ballpark,
12 I believe, so if you had 100,000 people every year, you
13 might expect about 17 new cases. So, even what can be
14 seen as large cohorts don't generate -- for other
15 outcomes don't generate large numbers. We haven't seen
16 many brain cancer patient studies out of the nurse's
17 health study. Maybe we will soon.

18 But a related question, some of these
19 large cohort both in North American and Europe and
20 other places that they already in place, they
21 periodically add new variables to their study. Now, I
22 don't know if they have reached a threshold of interest
23 in cell phones, but it might be worth asking if
24 anybody, any of these large cohorts that are in place
25 are collecting.

1 DR. ROTHMAN: That is a good point. But
2 to get back to your question about the numbers, let's
3 say you had 100,000 people who were heavy phones users
4 and 100,000 comparison people, if you are talking about
5 a doubling -- and I am not using that because I think
6 that is necessarily what we would expect, but it seems
7 to be a threshold of interest for many people, well,
8 then the 17 per year that you are talking about is
9 going to eventually be 34 a year instead of 17 and
10 picking it up won't be that difficult.

11 In fact, it suggests to me that you don't
12 need a cohort of 100,000 in each group. Then it could
13 be substantially smaller than that, perhaps 25,000
14 people who were heavy users or a cohort big enough to
15 perhaps have 25,000 people who were heavy users and
16 25,000 who light users and non-users, which would be --
17 it's still a big study, but it's a lot more tractable
18 than some of the huge cohort studies that we have seen.

19 We had the American Cancer Society study
20 one and study two and they were each a million people
21 that were followed over long periods of time. I think
22 we could do that with tens of thousands here with a

23 focused ascertainment.

24 I think the logistics really are very

25 manageable and still be able to answer the question in

1 a reasonable period of time.

2 DR. MOULDER: What is the duty of
3 statistics if by five years into the study a
4 significant of your light and non-users have switched
5 over into the heavy users category? Let them bias it a
6 bit at the start?

7 DR. ROTHMAN: You know, if you are
8 planning an experiment and you are asking the question
9 how should I apportion people into the new treatment
10 versus the comparison treatment, and if you are
11 interested in statistical power, the optimal is 50/50.
12 Everybody knows that, but that is actually true only if
13 there is no effect. If there is an effect, it's no
14 longer 50/50, though it doesn't diverge that much.

15 But if you have three in one group for
16 every one person in the other group, it actually
17 doesn't effect the power more than a trivial amount.

18 So, that kind of shift, unless it were
19 huge -- extreme -- probably wouldn't really effect the
20 study much at all.

21 DR. McBRIDE: One interesting aspect of
22 doing a study now, there may be non-users in the older

23 age groups and one of the issues has been that the
24 users have tended to be in the middle-age group and the
25 age of diagnosis for cancer, the average age is

1 somewhat older.

2 DR. ROTHMAN: That is a good point.

3 Because of that, what you would prefer to do is to
4 enroll people who are middle-aged users and then catch
5 them as they age into the age categories where brain
6 cancers are more common.

7 You might have the minimum age of 40, for
8 example to get into the study, which would be a
9 reasonable cut-off.

10 DR. MOULDER: Biologically that may make
11 sense, but politically it doesn't because there are --
12 for all the people worried about old folks getting
13 cancer from cell phones, there are an equal number of
14 people worried about young folks, so I think you are
15 trying to answer both political and biological
16 questions. I think you would like young users in the
17 study.

18 DR. ROTHMAN: I would argue against it. I
19 think it could be a separate study. You would really -
20 - it would really have to be thought of as a separate
21 study.

22 DR. McBRIDE: The issue of younger people
23 getting brain tumors, there are sort of two questions
24 there and that is whether or not you increase the risk
25 at the age in which people would normally get the

1 cancer. The second question is whether you are
2 reducing the average age at which they get it. That
3 came up with the ionizing radiation work.

4 DR. ROTHMAN: Most people think that the
5 childhood tumors that people get up through maybe the
6 late teens -- from birth through late teens -- are
7 really reflecting intrauterine exposures, so if you are
8 talking about teenagers using the telephone, then the
9 follow-up that we have to be talking about to do that
10 study would be many, many decades, so it would really
11 be a different study.

12 DR. OWEN: You were talking about the
13 various end points that have been mentioned in other
14 groups, and there was also cardiovascular malfunction.

15 DR. McBRIDE: Yes, that was in the report,
16 yes. And I wouldn't want to say -- these are not my
17 areas of expertise, but that report has a reference to
18 some of the literature on potential -- and again, one
19 would need to, first of all, have some justification
20 scientifically, but also it has to be something that
21 presumably is a health rather than and biological
22 effect and something sufficiently well defined and
23 reportable by whatever methods you use with this --
24 self-reports, the web based follow-up questions or some
25 other.

1 DR. BALZANO: Going forward, the addition
2 of some end points rather than tumors, would be very
3 good because, for example, if some pathologies are
4 going to come up, the study might as well embrace most
5 of the concerns that are conceivable, because
6 otherwise, the industry will find itself after
7 finishing with cancer, having to go on to something
8 else and then something else. If you can come up with
9 a large enough study --

10 DR. MOULDER: That is one of the big
11 advantages to the cohort study.

12 DR. BALZANO: Yes, I think in order to
13 make a good scientific study, we don't have much option
14 in terms of proposing a scientific study that will give
15 us some answers over a period of time. I don't think
16 there is anything else --

17 DR. MOULDER: One down side of a cohort
18 study is it doesn't give you an answer quickly.

19 DR. BALZANO: I realize that, but we have
20 got some of these other studies from Europe and so on
21 that will tell you that you are not dealing with
22 tobacco --

23 DR. MOULDER: I understand why it doesn't.

24 DR. ROTHMAN: But then it's not the cohort
25 study that you are talking about because if you are

1 talking about studying an effect that happens a long
2 time in the future, any study will --

3 DR. INSKIP: You can't study what hasn't
4 happened.

5 DR. ROTHMAN: Yes, you got to wait until
6 it happens to study it.

7 DR. MOULDER: I am just thinking that a
8 cohort study is going to be slightly harder to sell to
9 the public than a case control study, because you would
10 be telling them at the outset, we think this is the
11 right study to do, but we aren't even going to pretend
12 to have an answer for 20 years. It may not go over
13 very well. I don't think there is any way around. I
14 just don't think it's going to go over very well.

15 DR. INSKIP: In the meantime, here is what
16 we have.

17 DR. RINSKY: You will have an answer for
18 those are concerned that the disease occurs in a year.

19 DR. MOULDER: You already have that
20 answer.

21 DR. ROTHMAN: You have the IARC study to
22 give the answers in four or five years for short term
23 effects.

24 DR. MOULDER: I am not disagreeing with
25 you. I am just saying it's a little more of a selling

1 job. Of course, it also takes a long term funding
2 commitment, doesn't it?

3 DR. ROTHMAN: Yes.

4 DR. MOULDER: Decades long.

5 DR. ROTHMAN: Well, you know, it could --

6 DR. MOULDER: Or a decade long.

7 DR. ROTHMAN: Yeah, right.

8 DR. OWEN: In that timeframe, you can
9 predict what your costs are going to be -- more
10 reasonably than you could for some.

11 DR. ROTHMAN: I don't know. Sure, there
12 are a lot of unknowns in doing it, but if it's
13 something that obviously needs to be done, you get
14 started and you review your costs as you go along.

15 DR. McBRIDE: The Canadian report
16 recommended targeted funds for five to 10 years.

17 DR. RINSKY: As far as other outcomes to
18 look at, I think we should design the perfect storm
19 here. It's something where we can't quantify the
20 exposures and we really need an outcome like chronic
21 fatigue syndrome to run after forever -- so, we can
22 spin our wheels on that.

23 DR. BALZANO: Yes, if there can be some
24 pathologies that can be identified instead of some
25 subjective symptoms.

1 DR. RINSKY: That was my attempt at humor.

2 DR. BALZANO: I certainly appreciate it.

3 DR. MOULDER: But adding either ALS or
4 Alzheimer's to this -- I realize their diagnoses aren't
5 perfect, but they are not terrible either. It would
6 certainly be possible. Other cancers sound like they
7 would be fairly easy to add once you were going.

8 DR. ROTHMAN: Absolutely.

9 DR. MOULDER: Overall mortality would come
10 out automatically, right?

11 DR. ROTHMAN: Not exactly automatic, but
12 we could do it. If you could get Social Security
13 numbers, and I don't see why you couldn't, you could
14 certainly do a mortality surveillance on the cohort at
15 the same time.

16 DR. INSKIP: Are you aware of any sort of
17 pioneering web based cohort studies, ones that have
18 just gotten off the ground akin to what you are
19 proposing?

20 DR. ROTHMAN: I have heard of some and I
21 know of one that is being proposed in Sweden. I am
22 imagining that there are probably a lot of them that
23 are going on that I don't know about. Who is that
24 fellow in Pittsburgh who is doing all that web based
25 teaching? I bet he would know about it.

1 DR. MOULDER: There is no central registry
2 -- there is no organized way to find out what other
3 people are doing in this sort of area?

4 DR. ROTHMAN: I am guessing that if you
5 were attending the meeting in Toronto, the Epidemiology
6 Congress in June, you would hear all about it.

7 DR. MOULDER: Okay.

8 DR. ROTHMAN: And I'll be there, so I will
9 be looking for it.

10 DR. MOULDER: Great.

11 DR. OWEN: It sounded like to me when we
12 were talking earlier this morning about study designs,
13 I got the feeling that people thought we would have to
14 use all the available exposure assessment methods in
15 conjunction rather than picking one or another because
16 of their ability to inter-validate. Did I hear that
17 correctly? That we would need or try to include
18 questionnaires and billing records as well as sort of a
19 dose phone type pilot information.

20 DR. MOULDER: I think you need to include
21 billing records at least initially because you need to
22 get some handle on how much -- how long people had been
23 users before the day the study started.

24 DR. ROTHMAN: It's often the case that you
25 do it on a sub-sample. You don't need to do it for

1 everyone necessarily. You could do it on a selected
2 sample. It could even be a small sample just to
3 validate -- look at the correlation between that
4 information and other information and if it's
5 satisfactory, then you know you can rely on the other
6 information.

7 DR. OWEN: Certainly for the physical
8 measurements that would make sense, but I was wondering
9 if the technologies are changing, would you need to
10 revisit that validation step, again maybe in a sample
11 fashion?

12 DR. LOTZ: I'm not sure this is right for
13 us, but it would seem to me that if you can through
14 your updates track the changes in the technology that
15 they are using, you can use some other data and by that
16 I am thinking for example, people change phones. There
17 is now information on -- admittedly, it's limited to
18 one position and so forth, but there is evidence on the
19 SAR of a particular phone, so you would be able to at
20 least if you could track what technology changes they
21 were making, you would have some indications there that
22 you could do without having to rely ostensibly on
23 retesting or new instruments or that sort of thing.

24 DR. MOULDER: I think with billing records
25 -- you could design the study so that you were not

1 dependent on billing records. Once the study is
2 ongoing, your suggestion was you ask somebody how much
3 did you use in the last week -- assuming most people
4 can remember what they did last week.

5 DR. ROTHMAN: You can consult the last
6 bill and how many minutes a day the bill says --

7 DR. MOULDER: But this would be purely
8 voluntary on their part, which gets around a lot of
9 problems.

10 DR. OWEN: Yes, -- directly using the
11 billing records by prompting the individual to respond
12 --

13 DR. MOULDER: I think the most difficult
14 part of -- where you might need to use the billing
15 records is when you talk to someone initially enrolled
16 in the study who has been using cell phones for a large
17 number of years in different phones and different
18 companies to try to get a handle on how many years of
19 use they had on day zero of the study and I guess if
20 they kept all their billing records, you would have it
21 real easy. If they didn't, I -- guess you face the
22 same problems you do in any other retrospect to
23 epidemiology -- hope they are relatively unbiased in
24 their memories.

25 DR. ROTHMAN: There is a lot error

1 incorporated into those kinds of assessments.

2 DR. MOULDER: As you go further and
3 further into the cohort, the inaccurate information in
4 the beginning seems to me starts mattering less and
5 less.

6 DR. ROTHMAN: That's right.

7 DR. RINSKY: Say that again. The longer -
8 -

9 DR. MOULDER: When he is 10 years into his
10 study, for the last 10 years you have really good
11 records for their use and the part where you had to
12 rely on memory is now 10 years ago.

13 DR. BALZANO: At that point, you got a
14 pretty good idea for patterns of usages.

15 DR. McBRIDE: This other sub-set could be
16 done to validate self-reporting. If there was an
17 interval of six months, it seems one might be
18 interested -- and you asked for the last week of use,
19 which usually gives you better recall. You can also do
20 smaller studies, too, and see how that might vary from
21 three months ago or one month ago. And those again
22 need only smaller studies to give you some of the

23 variability.

24 DR. MOULDER: Would there be any political
25 problems or ethical problems if when you enrolled

1 people in this study, you told them as a condition of
2 this they would have to occasionally give you billing
3 records?

4 DR. ROTHMAN: I think it would be a
5 practical problem. You wouldn't have much control over
6 the proof.

7 DR. MOULDER: It seems to me, if five
8 years into the study, you want to validate by asking
9 for billing records, some people would be willing to do
10 it and some people wouldn't and it might be a biased
11 set.

12 DR. McBRIDE: I'm just thinking, what you
13 want to do is correlate a self-report --

14 DR. ROTHMAN: Well, people who have
15 billing records and are willing to give them to you
16 might be people who are more meticulous about
17 everything they do. That's possible. Don't forget
18 that you shouldn't look for a level of accuracy that is
19 going to go beyond the level of accuracy that is going
20 to relate to all the other aspects of the study, so I
21 think you only need to go so far.

22 The epidemiology is actually pretty good

23 at finding the facts, even with really simple
24 questions. If you look at the historical record, there
25 is always debate about some things that may be false

1 positives, but things that we know are real effects, we
2 do find in epidemiologic studies, sometimes with
3 surprisingly crude questions, so I think that kind of
4 information that we are talking about ought to be
5 adequate to deal with this.

6 DR. LOTZ: I would think too rather than
7 have to ask people for billing records, you could do
8 something like Q. was talking about with the technology
9 where you could get somebody to use a dosimetry phone
10 for a month rather than give you the billing records.

11 DR. OWEN: Could be a lot better.

12 DR. LOTZ: A lot better information really
13 that could periodically do a sub-set that would
14 validate that things were still standing up to
15 reporting and just free you from trying to go after
16 those billing records.

17 DR. ROTHMAN: And you can also provide
18 incentives for people to come up with billing records,
19 which reduces the selection of people.

20 DR. BALZANO: Yes, there are ways around
21 it.

22 DR. MOULDER: What is the initial

23 motivation for these 50,000 people to come on board --
24 for 100,000, whatever it is?
25 DR. ROTHMAN: Ideally, you want to get

1 people who are just committed to the idea of just being
2 in the study, which is very few people, I think, meet
3 that condition, but those are the people you want. So,
4 if you can -- the less inducement you use, the better,
5 because that way you get people who are willing to be
6 in the study.

7 DR. MOULDER: So, you advertise basically?

8 DR. ROTHMAN: One way or another. You
9 might use web based advertising, first of all, that
10 would get to the people that you want to include, which
11 would be people who have contact with the internet.
12 There are already websites that I have visited on a
13 couple of occasions that are there to enroll people in
14 various kinds of studies. And what they do is they ask
15 you questions -- are you interested in being part of a
16 project that will help determine what the health
17 effects might be from a variety of things that you
18 experience in your life. There are people who want to
19 do that.

20 DR. OWEN: Everybody gets one of those
21 bills in the mail, too. Their cell phone bill -- is
22 another way to reach them. It's not necessarily going
23 to select out the ones who are good for web access, but
24 if the first thing it says is if you are interested, go
25 to this website to learn more.

1 DR. RINSKY: That would select them.

2 DR. OWEN: Earlier, I think you said
3 something, Q., about the -- I'll phrase it differently,
4 but kind about the window of opportunity for doing --
5 for starting such a study, based on the technology that
6 is being used right now, when it's going to change. I
7 was wondering if I could get more discussion about
8 that.

9 DR. BALZANO: The so called QNF, third
10 generation, I don't know how rapidly they are going to
11 come. There is a major transition in technology in
12 that there is more information to collect, you have a
13 different exposure area. So, I don't know how rapidly
14 the third generation is going to come to this country.
15 I think it's going to be slower than Europe and
16 certainly Japan. That is my impression and probably
17 Jo-Anne can tell us more about it, but that is my
18 personal view, at least right now, just because of the
19 fact that people don't seem to be banging on the doors
20 of the suppliers.

21 So, we have a window of opportunity right
22 now to get some more information about the current
23 technologies before the QNF and the 3-G technologies
24 come in, where you would end up with different
25 instruments. The phone will probably become a display

1 phone instead and have a bigger screen to add into the
2 discussion.

3 So, eventually you are going to face that
4 transition, but I think now we have a period of time
5 before this type of technology is widely introduced to
6 the public and that would give us a window of
7 opportunity in order to study the technologies of
8 today, the last few years.

9 We will have new phones, new displays, new
10 ways to hold it. It will be substantially different.
11 It is very difficult to use the web with this display.
12 The display is going to have to be much bigger and the
13 phone would have to become bigger, so I expect the
14 dosimetry to be radically different.

15 Again, my opinion. Remember that I don't
16 represent anybody any more.

17 DR. RINSKY: I just had another thought.
18 It might seem a little far-fetched at first, but
19 another potential drawback to the prospective study is
20 if you look at it for the first time at five or 10
21 years and we have -- we see a very non-significant
22 excess such as 10 or 15 percent, then what do you do

23 about your study? Do you tell everybody there is an
24 excess of 10 or 15 percent or do you continue the
25 study? You have some ethical issues that you better

1 figure out ahead of time before you encounter that.

2 DR. ROTHMAN: Why would you discontinue
3 the study?

4 DR. RINSKY: You would say we have 15
5 percent, we are telling everybody now that you better
6 alter your habits and we are telling manufacturers that
7 you have better change your equipment. Not that it's
8 statistically significant -- not that it couldn't be
9 just a spurious answer --

10 DR. OWEN: The regulatory policy could
11 have an effect on your study.

12 DR. RINSKY: On your exposure. I assume
13 you report as 20 or 25 percent, somebody is going to
14 get very jacked out of shape because they are not going
15 to understand --

16 DR. MOULDER: I don't think it makes you
17 terminate your study. It may change the usage pattern
18 in some of the members of it.

19 DR. RINSKY: Did I say terminate? Alter
20 would be better.

21 DR. INSKIP: And did you say report
22 earlier than you would otherwise?

23 DR. RINSKY: But reporting it in and of
24 itself is either going to change your study --

25 DR. INSKIP: If you had a 10 or 15 percent

1 excess, you really don't have much information to
2 report.

3 DR. RINSKY: I quite agree, but your
4 participants and any IRB would require you to
5 periodically reveal any results you have upon being
6 asked by any participants and they are going to be
7 interested in the 20 percent.

8 DR. MOULDER: That would not require us to
9 report to the patients an outcome unless it was
10 approaching statistical significance.

11 DR. RINSKY: I don't know. I am saying
12 these are --

13 DR. MOULDER: Well, I do clinical trials
14 and we don't have to -- you have to do the periodic
15 interim analysis and if the people on your drug are
16 doing worse, at some point, you have to tell them, but
17 just a non-significant indication that something may be
18 happening does not trigger a reporting requirement.

19 DR. RINSKY: Okay.

20 DR. ROTHMAN: And also I believe that it
21 would be out of place for the investigator to be making
22 recommendations about regulatory policy in the same
23 paper that is supposedly reporting the findings.

24 DR. MOULDER: And certainly, if this is
25 done in this country, everybody doing this is going to

1 be doing it under some institutional review board that
2 will presumably require them to have some interim
3 analysis and require them to have notification rules if
4 things happen.

5 DR. RINSKY: That's what I was talking
6 about.

7 DR. ROTHMAN: No, interim analysis is a
8 feature of clinical trials. It's not a feature of non-
9 experimental studies.

10 DR. MOULDER: Oh, I didn't know that.

11 DR. ROTHMAN: Because you are not
12 delivering the phones to these people and making them
13 use them. It's something they are doing on their own.
14 So, you don't have any requirement to do safety checks.

15 DR. MOULDER: But this would have to go
16 through IRB.

17 DR. ROTHMAN: Yes, they are worried about
18 confidentiality and things like that. They are not
19 worried about your harming your study subjects.

20 DR. McBRIDE: It's strictly an
21 observational study.

22 DR. MOULDER: And if as part of
23 observations you come up with something that indicates
24 a threat to the subjects, you don't need to tell them?

25 DR. ROTHMAN: Well, if you do a study of

1 smoking and pancreatic cancer and you find that there
2 is a result, you have a public health responsibility to
3 make the results known. You don't have a deadline.

4 DR. McBRIDE: I mean, this goes back to
5 the criteria for causation and evaluation of risk
6 assessment. Again, no single study, even a large US
7 cohort study is definitive. One needs replication, all
8 the criteria --

9 DR. RINSKY: Mary, you are trying to
10 explain something to me. I'm in the choir.

11 DR. McBRIDE: I guess I don't understand -
12 -

13 DR. RINSKY: What I am saying is if you go
14 through Center for Disease Control IRB and you say that
15 at five years or at 10 years, I am going to calculate
16 an SMR, they are going to say -- I am telling you, that
17 IRB, I don't care if it is an observational study, they
18 are going to say, and what are you going to do with
19 those results? How do you plan to inform the
20 participants in your study?

21 DR. ROTHMAN: The answer is to publish
22 them in a scientific journal.

23 DR. LOTZ: One thing, Bob, that I was
24 thinking, too -- I mean, right now, we are meeting to
25 decide whether such a study is a good idea. If you got

1 that kinds of results, I don't think you would have
2 that debate any more. Yes, it would alter your study,
3 but you would actually increase and maybe even do other
4 confirmatory studies. So, in that respect, it would
5 have a positive feedback on what you were trying to
6 accomplish.

7 DR. OWEN: I guess if I have been
8 understanding the possible way that this could be
9 approached, then certainly you might expect the release
10 of that kind of information to affect your usage
11 patterns, but you are still collecting the information
12 about the usage patterns. So, you are still going to
13 be able to tell what is going on.

14 DR. ROTHMAN: I don't know how much it
15 would affect it.

16 DR. OWEN: Yes, it might not at all.

17 DR. ROTHMAN: The Surgeon General's report
18 was issued in 1964.

19 DR. RINSKY: Yes, but that was a real
20 problem.

21 DR. OWEN: If there were some in your
22 cohort that maybe were going to change their usage

23 patterns, that would show up in maybe six-month
24 intervals of checking with them. So, what it sounds
25 like to me is maybe there could be such an effect that

1 you would describe, but it seems like it wouldn't hurt
2 the conduct of the study.

3 DR. RINSKY: I was thinking maybe in terms
4 of what would be required by the investigators to do if
5 they began to see a positive effect earlier on in the
6 study -- not so much what would the public reaction be
7 to that. Although there would be. There are advocacy
8 groups and you have better believe they would make hay
9 out of some minor thing.

10 DR. ROTHMAN: But I think the model you
11 have in mind is that of a trial where you have to worry
12 about these things.

13 DR. RINSKY: It really isn't, Ken. At
14 NIOSH we have a right to know policy that has been
15 worked out over years and it's extraordinarily
16 suffocating and you will spend three, four, five times
17 as much informing every subject in an observational
18 study of what you don't know at the end of the study
19 than you would for what it costs to do the study in the
20 first place. It's gotten that --

21 DR. ROTHMAN: But this is not a generally
22 applicable rule, is it?

23 DR. RINSKY: It's generally applicable
24 through a whole branch that does nothing but that.

25 DR. INSKIP: For outside institutions.

1 DR. ROTHMAN: Yes, no one else has to do
2 that, just your place.

3 DR. RINSKY: I agree, but it's -- well, I
4 don't know. NCI got raked through the coals plenty on
5 not releasing the iodine studies and not making a big
6 to do about it. It was the same argument.

7 DR. INSKIP: I don't think there has been
8 individual call backs. There has been papers and
9 various informational things put out.

10 DR. RINSKY: There was a congressional
11 hearing on how they handled the data.

12 DR. INSKIP: There wasn't an IRB mandate
13 to go out and contact every person who might have been
14 affected by fall out and tell them --

15 DR. RINSKY: What happened?

16 DR. INSKIP: I wasn't part of that
17 process.

18 DR. RINSKY: We all know what happened
19 from the national news. What happened to those very
20 fine scientists who discovered things earlier on and
21 were perceived to be late in warning every single
22 person? They got creamed.

23 DR. GRAJEWSKI: NIOSH has a notification
24 policy which does kick in. There are some fairly
25 straightforward algorithms and we try to do

1 communication of results at levels of results that are
2 not as notable in terms of findings, but generally with
3 the exception of reporting medical results, the
4 communication efforts are done on a group basis rather
5 than individual basis and notification of individuals
6 doesn't kick in unless you have fairly meaningful
7 results to communicate.

8 DR. INSKIP: Presumably, would the IRB
9 involve -- it would just be the IRB at the center of
10 the PI? Would that be -- is that the only IRB that
11 comes into play?

12 DR. OWEN: It could be anything I think,
13 because the grant paradigm is not necessarily --
14 complete guidance in this case. Everything about this
15 process, the things that are coming about through the
16 cooperative research agreement are a little unique, so
17 potentially FDA could express an interest in having a
18 notification policy of some sort that was custom.

19 But it's also possible that a grant
20 paradigm could be used and you could just simply say
21 make sure you got an IRB and your IRB is happy with how
22 you are going to do things and setting things up and,
23 by the way, tell us what that is.

24 DR. ROTHMAN: I'm not so worried that
25 whatever the rules may be for NIOSH, we don't need to

1 project them to this particular problem. I published a
2 paper a new years ago on teratogenicity of vitamin A,
3 an arguably important connection that people --
4 especially women of childbearing age would need to know
5 about, but there were never any rules in conducting my
6 research that applied to how I would report them, when
7 I would report them, whom I should notify. I had the
8 advantage of not working a government job in doing this
9 research, so I didn't have to face any of these rules.
10 I just published by results and then everybody
11 criticized it.

12 DR. OWEN: It's an interesting thought.
13 It's a little bit early to deal with it because we are
14 a few steps upstream from knowing whether and what will
15 be recommended and whether that will be conducted by
16 government groups.

17 DR. RINSKY: Conducted or funded. I think
18 funding is the issue here.

19 DR. OWEN: We know where the funding is
20 coming from. It's not the government. It's the other
21 half.

22 DR. RINSKY: That is a real advantage --

23 as far as projecting NIOSH's problem on the rest of the
24 world, this was not homegrown at NIOSH. This resulted
25 from interested parties, primarily my understanding is

1 some plaintiff lawyers who thought that people had a
2 right to know and they pushed it until there were the
3 appropriate congressional pressures to cause that
4 agency to adopt what a lot of people in the agency
5 didn't agree with. Same thing could happen very easily
6 with FDA.

7 DR. ROTHMAN: Well, the occupational
8 setting may actually be different in terms of
9 notification than the kinds of settings that would
10 apply more broadly and that might be applicable to
11 cellular telephones.

12 DR. MOULDER: Well, I think this would be
13 an issue to take into account designing this still
14 mythical study, but I don't see any way that it would
15 prevent it from being done. I just think whoever does
16 the design, whosever IRB this goes to has got to think
17 about this one and decide what they are going to do, if
18 anything that could be seen and threatening comes out
19 of it and under whose rules.

20 DR. ROTHMAN: But the way you pose the
21 question, you made an excellent point -- the fact that
22 you could have a finding that is something to be
23 skeptical about for a variety of reasons. What would
24 be the guideline other than scientific judgment of what
25 to do with that? More analyses to do, perhaps wait for

1 more data to come along. These are scientific
2 questions. They are not really regulatory or questions
3 that are public health questions.

4 DR. OWEN: Actually thought, I think in
5 the situation that we are talking about here, for
6 studies that would come out of this project, there is a
7 -- I think it's reasonable to expect that FDA would
8 have access to all the data as the study went along,
9 all the analyses of them as the study went along.

10 And FDA then on it's own would have to
11 make calls like that, but it would be something that
12 necessarily you would have set up beforehand. It would
13 have to be at the moment. FDA might decide that there
14 is information of public health import that needs to
15 made publicly available, but in that case, it could
16 sort of be taken out of the hands of the investigators
17 depending on what the information is.

18 DR. ROTHMAN: There might be a reporting
19 requirement to the FDA.

20 DR. OWEN: Oh, there will certainly be a
21 reporting requirement at many stages.

22 DR. BALZANO: But it's true, it will be up
23 to the FDA to make that call.

24 DR. ROTHMAN: And that wouldn't be bad.
25 The FDA is very responsive.

1 DR. MOULDER: Otherwise known as not our
2 problem.

3 DR. ROTHMAN: No, it is different. If you
4 are reporting to the FDA, that is not the same as
5 making your own decisions about publication. I have
6 been involved in that situation and I know that puts a
7 different kind of pressure.

8 (Dr. Bassen enters.)

9 DR. OWEN: Hello, Howard. Glad you made
10 it. You are in time for us to break for lunch. Do we
11 have any commitments that we are bound to or can we
12 have our lunch any time we want?

13 DR. BASSEN: Have you gotten into
14 engineering yet?

15 DR. OWEN: No, you are in luck. We
16 haven't gotten too much into it. There has been
17 occasionally use of incorporating dose measurements
18 into studies, but we haven't gotten into the nuts and
19 bolts of it.

20 Actually, I think we will just go ahead
21 and break for lunch now. I think that an hour and half
22 ought to be enough for people or is that too much? I
23 am not sure how crowded the restaurant is downstairs.
24 I think an hour an half. I have got 12:15 now, so that
25 is 1:45.

1 (Recess for lunch.)

2 DR. OWEN: Did we get everybody back? I
3 was going to start off the afternoon by touching on a
4 few things that we hit this morning and bringing them
5 back up again to try and get a little more input.

6 One of them was that there was a mention
7 of the possibility of adding on to existing large
8 cohort studies and adding on variables. And I wondered
9 if people had anything more to say about the
10 feasibility of such an approach, the likelihood that
11 something like that might be done and comments either
12 in isolation or in comparison to a prospective study
13 design for the express purposes of looking at phones.

14 DR. MOULDER: I don't think any of the
15 existing cohort studies are going to be web based. I
16 think they are all too old for that.

17 DR. ROTHMAN: No, but if they are going
18 through the procedures that they are going through,
19 then one of the main advantages of being web based
20 becomes moot.

21 DR. MOULDER: I thought one of the big
22 advantages of web base was keeping the data base up to
23 date, not just recruiting people.

24 DR. ROTHMAN: These studies are still in
25 contact with people on a regular basis. At least that

1 is what I assume you are talking about. So, they would
2 be accomplishing that, but they may be doing that in
3 another way, probably by mail questioning.

4 I think the real problem with doing that -
5 - there isn't many big problems with doing that. If
6 somebody is willing to do it, fine, but since this
7 would be an add-on, it's unlikely to get the full
8 attention of the investigators in the way that it would
9 if it were the primary objective of a study.

10 So, you will be competing with other
11 people who want to put their questions in on the
12 questionnaires. And also you would have to be starting
13 now and then the question is how long is that cohort
14 going to continue. How many more years is it going to
15 be funded since it's not funded for this purpose.

16 So, the risks are that it will peter out
17 too soon because this isn't the objective, that you
18 would compete against too many other issues that would
19 be trying to work their way into the questionnaire and
20 therefore, you might have to settle for just a couple
21 of questions and wouldn't get the full detail and the
22 benefit of the validation that we have been discussing.

23 On the other hand, it would be
24 comparatively cheap and easy to do compared with the
25 kinds of studies that we have been discussing.

1 DR. GRAJEWSKI: Cheap and easy if you
2 latch onto an existing surveillance such as in Hanes --
3 it's to the tune of about a million dollars per
4 question from what we were able to find out. They will
5 add questions to a repeating health surveillance of
6 that nature, but the cost is prohibitive and your point
7 regarding how many questions and what quality and
8 competition are certainly valid there.

9 DR. OWEN: That is for a cohort of what
10 size?

11 DR. GRAJEWSKI: It's large. I forget the
12 exact size.

13 DR. MOULDER: It's not just a matter of
14 asking questions. You would also have to get some
15 detailed history of their past phone use at the start
16 of the study, which would be more an a couple of
17 questions.

18 DR. ROTHMAN: I was thinking for example
19 if you could graft this onto the health professional
20 study, which is a fairly sizeable ongoing cohort study
21 up in Boston of tens of thousands -- maybe close to
22 50,000 or more male health professionals.

23 The problem is that study started in '86
24 and I don't know how many more years it's going to run
25 and they send out questionnaires periodically, but they

1 are not going to devote the space to getting a full
2 detailed history. I would very much doubt it anyway.

3 DR. MOULDER: It might also be a group
4 with extraordinarily high penetration of phone use.

5 DR. McBRIDE: Depending on the age range.
6 That was one thing I was going to comment on. You want
7 your cohort to be one that would be formative and have
8 a reasonably high prevalence of cell phone use.

9 DR. ROTHMAN: So, these are all good
10 objections and that means that there would be
11 compromises to offset the benefits.

12 DR. OWEN: Another thing that came to
13 mind. I think you made one comment about your idea or
14 sort of a minimum possible cohort size that would be
15 useful. I think you said something like 25,000 each of
16 the high users versus 25,000 non-users.

17 DR. ROTHMAN: That may be a little bit
18 low, but in the 25,000 to 50,000 range.

19 DR. OWEN: Yes, I was wondering if anybody
20 else had any thoughts about that in terms of the size
21 of the study that might likely be desired, the size of
22 the cohort that might be desired to look into this kind
23 of thing.

24 I realize that we are not talking about
25 trying to figure out what the power calculations are

1 without knowing all these variables, but just back of
2 the envelope estimates like that one.

3 DR. MOULDER: In the study that you had
4 started, what did you figure your cohort size would
5 have to be?

6 DR. ROTHMAN: Well, it's a slightly
7 different set of circumstances. It was basically a
8 little younger cohort than the cohort that we are
9 talking about here. It was much shorter follow-up.

10 DR. MOULDER: But that would sort of place
11 an upper limit. If that was going to work with a
12 younger cohort and shorter follow-up.

13 DR. ROTHMAN: We were looking at a million
14 people --

15 DR. MOULDER: Oh.

16 DR. ROTHMAN: -- in the exposed group and
17 then we actually had -- see, we had the advantage of
18 taking a cohort from the days when about half the
19 people or nearly half -- maybe more than half -- maybe
20 had car phones and their only cellular telephone, which
21 meant that there exposure was essentially zero, but the
22 use patterns were similar.

23 DR. MOULDER: So, it's not possible.

24 DR. OWEN: Well, now that we have Howard
25 with us, I thought maybe I would try and get people to

1 turn more exclusively to discussing exposure assessment
2 issues for a while. I thought maybe, Howard, you could
3 start raising points as you saw fit and maybe get
4 discussion from there and at the end of the day, Dr.
5 Lundquist has volunteered to make some comments for us
6 on the topic of exposure assessment as well.

7 DR. BASSEN: Well, knowing nothing about
8 which bio effect you are going to be focusing on,
9 supposing we have a specific study, the premise that
10 most modern bio effect research is based on is a dose
11 response in terms of specific absorption rates -- not
12 exposure, but absorbed dose and not even absorbed dose,
13 but a distribution of absorbed dose in different
14 organs, none of which there is any laboratory research
15 that points out is more suspectable than others if we
16 are talking about something other than heating.

17 I won't address any of the bio effects
18 issues, just to recommend that specific absorption rate
19 distribution be estimated in any users and that that is
20 a function of many variables.

21 I'm chairing a committee of IEEE on SAR
22 determination for certifying cellular phones and we
23 found that different distances of a centimeter can
24 cause a change of 100 percent in the SAR. That means
25 if the phone is moved one centimeter away from another

1 position that it formerly occupied, the SAR or the
2 point in the head where it's maximum is reduced by at
3 least a factor of two.

4 So, with that much variability, you should
5 understand that we are not going to get a measure of
6 dose that is anything but an order of magnitude and
7 then to try and predict where it is will depend on the
8 user's position in terms of how they hold the phone,
9 whether their hand is on it or not, in terms of the
10 antenna -- whether the antenna is up or down, so it's a
11 very difficult issue to quantify.

12 I would just say that if there are some
13 suggestions, ways other than measurement technology
14 called dosimetry that could be used, that would be a
15 good thing to consider -- like position of the handset.
16 And since every handset will not only be certified in
17 terms of SAR in a model of human head, at least you can
18 get some order of magnitude estimate for each phone of
19 the distribution throughout the head of SAR. So, that
20 data should be utilized and the FCC will be collecting
21 that data.

22 DR. OWEN: So, actually that kind of gets

23 right to the question I was getting ready to ask. Was
24 there things in dosimetry or exposure assessment that
25 are likely to be doable in the short term and should be

1 done before we try and go anywhere with the study?

2 DR. BASSEN: Well, there are lots of data
3 sets on SAR distribution in the head of handset users,
4 both from measurements and from computations and, as I
5 said, the FCC will be collecting those -- they already
6 are -- for every manufacturer that sells phones in the
7 US.

8 Q., do you know how far back that
9 certification -- since '97 or something?

10 DR. BALZANO: Yes, it started in probably
11 '97.

12 DR. BASSEN: So, if you can identify the
13 model of the phone, you have a relatively good estimate
14 of the range of SARs, but the types of SAR depend on
15 the phone operating characteristics. Not the antenna
16 and that kind of thing, but if it's digital or analog
17 and I am not even addressing the base station proximity
18 issue. Everything I am talking about is with the phone
19 output at its maximum value. I am assuming that you
20 have the technology to track output power by some means
21 where the base station records radiated power.

22 So, I would recommend that you work
23 closely with the FCC to get information on the specific
24 phone SAR distribution as well as the manufacturers of
25 phones and that you try to identify the phone model and

1 manufacturer carefully instead of just a digital phone
2 -- and you should know what brand and model it is.
3 That may be impossible. I don't know.

4 DR. MOULDER: All the phones since '97 or
5 so do have a unique FCC ID number on them, don't they?

6 DR. BALZANO: Sure, they have an ID
7 number. There is an ID for each phone. Now, in terms
8 of acceptance standards from the FCC --

9 DR. MOULDER: No, I am just suggesting
10 that since many people don't know what model their
11 phone is --

12 DR. BALZANO: Oh, yes.

13 DR. MOULDER: -- if you can people to open
14 the battery case and tell you what the FCC ID number
15 is, you would know.

16 DR. BALZANO: Oh, certainly.

17 DR. ROTHMAN: How would you know?

18 DR. BALZANO: There is a number --

19 DR. MOULDER: Well, assuming that they
20 read the number correctly.

21 DR. BALZANO: Yes.

22 DR. MOULDER: Each phone has an ID number
23 coded to the FCC data base that tells you which phone
24 model it really is, not what you think it is.

25 DR. ROTHMAN: The FCC data base is

1 available?

2 DR. MOULDER: He is showing you. On your
3 phone, you can get a unique FCC model number off it.

4 DR. BASSEN: And then the manufacturer
5 would be able to tell you what kind of SAR is
6 associated with it.

7 DR. MOULDER: And even what kind of phone
8 it is.

9 DR. BALZANO: You should be able to access
10 the FCC network. The FCC has a website --

11 DR. MOULDER: Only on the newer phones.
12 On the older phones where the information is on paper,
13 that is not on the website and apparently, their
14 efforts to retrieve it from their file cabinets has not
15 gone well.

16 DR. BALZANO: I thought that eventually
17 the FCC was going to put their entire data base on the
18 --

19 DR. MOULDER: My most recent is that they
20 have kind of given up putting -- get the old stuff off
21 paper and onto the data base. The issue is old phones
22 that is not going to help. If the phone is old enough
23 that the person doesn't have it, you are not going to
24 get a model number. But most of the modern phones, if
25 they look up the data base. With the old phones, it's

1 going to be tough.

2 DR. ROTHMAN: Old meaning since what year?

3 DR. MOULDER: Certainly pre-'97 it would
4 be tough and pre about '99 or so, it's not in the
5 electronic website.

6 DR. OWEN: Or at least it's not
7 comprehensive. I looked up a very old phone there --
8 it's a PDF of the type -- acceptance certificate was
9 actually a phone from 1996, but like I said, it must be
10 spotty.

11 DR. BALZANO: Yes, I think so. Again,
12 since August 1996 it became mandatory, so previous to
13 that it was voluntary, so you might find that some
14 companies filed some of the information with the FCC,
15 but it was on a voluntary basis and you will find that
16 it's not going to be the majority of phones.

17 DR. MOULDER: In addition to which, that
18 number is the worst case SAR and I don't know how the
19 worst case SAR corresponds to reality and it's going to
20 take dose phones in Europe to tell you what the
21 relationship is.

22 DR. LOTZ: I think there is enough

23 uncertainty in that testing that that is a very big
24 factor.

25 DR. BASSEN: Well, it's probably a factor

1 of four for the old phones maybe, but what we are
2 talking about is a hot spot, one gram, one cubic
3 centimeter and if there is a bio effect, what are --
4 are you looking for that bio effect in that temporal
5 region? That is all you are going to get, because
6 everything five centimeters away is down to pretty much
7 zero does. So you have to realize that we are talking
8 about just a very focused small area that has any SAR
9 if you were to draw the equi-dose contours.

10 DR. OWEN: So, you make it --

11 DR. BALZANO: Along with a peak SAR
12 average -- whatever number of grams -- normally there
13 is a map that goes with it that can give you a pretty
14 good idea of the exposure of the entire side of the
15 face. I don't know if the FCC has actually put that
16 information on the website, but the FCC does require
17 the entire mapping. There is a lot of information
18 there on exposure.

19 DR. BASSEN: Do they also give the 10 gram
20 average?

21 DR. BALZANO: That's correct. If you use
22 that system spec, it will give you the (inaudible) in
23 one gram and 10 gram averages.

24 DR. BASSEN: But does the FCC have 10 gram
25 average?

1 DR. BALZANO: I don't know. When we find
2 out how it became all of a sudden one sided -- because
3 that is my experience -- but normally when we provide
4 the information to the FCC, the is the entire printout,
5 the printout with numbers. We file into the paper only
6 the one to the FCC, but if you look at (inaudible).

7 DR. BASSEN: Well, I would recommend that
8 one thing that should be done for an epi study would be
9 to get the spacial maps of the most common phones and
10 get an idea of where the dose is concentrated, so that
11 people will know what they are dealing with in terms of
12 exposures to the tissue.

13 DR. OWEN: What is the relative -- and if
14 you get two sorts of variation in SAR and you have got
15 model to model variation, but then you have got all
16 these other factors that are more pattern of use --
17 that are positioning factors --

18 DR. BASSEN: Model to model -- you mean
19 different model numbers?

20 DR. OWEN: Yes, sorry.

21 DR. BALZANO: Different models in the same
22 brand.

23 DR. OWEN: Model A versus model B. Is the
24 variation due to the position of use large with respect
25 to the variation from model A to model B and model C?

1 And, if so, is it so large that the difference between
2 the different models is less important, unimportant?

3 DR. BASSEN: I don't have that information
4 because at FDA we don't look at that, but the
5 manufacturers and the FCC certainly do and I would
6 suspect position is a big factor.

7 DR. MOULDER: There is another factor in
8 addition. The other factor is your distance from the
9 base station.

10 DR. BASSEN: Right.

11 DR. MOULDER: The phone adapts to the
12 distance and that can be about a factor of 10, maximum
13 to minimum?

14 DR. ROTHMAN: No, it's almost 100.

15 DR. BASSEN: But I thought that could be
16 handled as a separate issue by the base station data
17 records if they record received power. I don't know.
18 I understood they did.

19 DR. MOULDER: I don't see how we could
20 possibly acquire that data if we were in the big cohort
21 study.

22 DR. BALZANO: You don't take it in a big
23 cohort study. You collect the statistical data by just
24 sampling a certain number of the dose phones in the
25 population.

1 DR. INSKIP: How much good does a lot of
2 the real detail from micro level dosimetry do if you
3 cannot locate the site of origin of the tumor with a
4 comparable degree of accuracy? You go and try and get
5 MRIs of tumors and recruit the services of neuro-
6 radiologists, but by the time the tumor is diagnosed,
7 if it's four inches in diameter, just assume the cell
8 of origin was in the middle and I think before one gets
9 too far into some of the micro regional variation of
10 dose within the cranium, one has to be contemplating a
11 design where one is going to get pretty high resolution
12 information on location of the tumor beyond left or
13 right.

14 DR. MOULDER: I am not sure how much that
15 would help, because I think by the time you are done
16 with this, the typical person in the study who develops
17 brain tumor may have used three or four or five models
18 of phone over their careers, each of which would have a
19 different SAR pattern and you would be shooting in the
20 dark.

21 I think the real thing that came out of
22 these comments is how important is it going to be to
23 know which phone people had or is the dose they got so
24 much determined by other factors that the model to
25 model variation is going to be essentially useless

1 information.

2 DR. INSKIP: Maximum power doesn't really
3 tell you at all what you need to know, I don't think --
4 the operating characteristics in the phone, if the
5 phone is really operated at that power which they are
6 rated on.

7 DR. MOULDER: So, I am going back to your
8 comment. The best you may be able to do is separate
9 heavy users from light users and the rest of this may
10 be so variable as not to be helpful.

11 DR. BASSEN: I think it would be
12 worthwhile doing a study though, an analysis of that
13 issue, a systematic analysis of all of the variables to
14 highlight the most significant ones, whether it's
15 handset position or model number or base station to
16 phone handset proximity.

17 DR. MOULDER: Is this what the dose phone
18 study out of Europe is supposed to accomplish?

19 DR. BALZANO: Yes, it's supposed to give
20 definitely some of the answers, not all of them. You
21 have to remember that there is no such a thing as an
22 antenna on the cell phone. The entire cell phone is
23 the antenna. We need to establish that, okay?
24 Depending on how you position it, you get a radical
25 variation. Even a can push of one centimeter can cause

1 -- for example, in this particular case, the most
2 exposure comes out of this area. That is why when you
3 change phone, depending on how the printed circuited
4 board, the assembly of the phone, has been done by the
5 manufacturer, you get different pattern on the
6 position. Such is life. I mean, it's very simple.

7 DR. MOULDER: Would you be advocating that
8 a dose phone type study be done in the US as a
9 preliminary to such a --

10 DR. BALZANO: My suggestion would be yes.
11 That is pretty much what I already suggested. We are
12 talking about a major effort -- a prospective study,
13 the cohort. This is going to entail a substantial
14 amount of funding and a portion of the funding towards
15 a good dosimetric evaluation. So, we have an idea, for
16 example, if a person is in a densely populated area
17 where you get a lot of base station, what is the
18 average power? Obviously we are looking at the
19 statistics. We are not looking at individuals.

20 But if you add people in large urban areas
21 and they have other base stations, chances are that
22 most of the time, the phone is used in a minimum power.

23 DR. MOULDER: Do you expect the dose phone
24 study done in the US to provide different information
25 than the European one? Is the pattern of use that

1 different?

2 DR. BALZANO: It's not so much the power -
3 - not the pattern of usage. If you look at the
4 topography and at the height of the buildings -- that
5 is where I think -- and that is why I am advancing this
6 idea.

7 DR. MOULDER: So, it might be different in
8 the US?

9 DR. BALZANO: It might be different. I
10 don't know how much. But if you are going to hopefully
11 back this long term prospective study, this will be an
12 essential step, collecting data, and then you can use
13 the data for statistical purpose and also for the
14 evaluation of whatever questionnaire that you are going
15 to be using.

16 DR. MOULDER: So, you can imagine that for
17 doing a study, you might discover that it was important
18 to know if the person used their phone in an urban or
19 rural area conceivably -- or in a car or not in a car
20 or in an office or out in the open. It could make as
21 much difference as the phone model conceivably.

22 DR. BALZANO: If you are in the car for
23 example, okay, and you are going around town, the
24 exposure is much higher than if you are walking. The
25 signal has got get around the car. And if you are

1 walking, it's really a determined angle. If you are
2 walking around a corner, your exposure goes up or goes
3 down substantially.

4 It means nothing to collecting data to
5 make sense unless you know what you are doing and for a
6 marginal expenditure, I think we might buy a
7 substantial amount of additional knowledge that would
8 help the epidemiologists get around to extract the
9 exposure surrogates that makes much more sense than
10 just exposure and that's it -- and phone time.

11 So, in the pattern of usage also should be
12 investigated is to find out if people use on the right
13 and some people use it on the left. Using it on the
14 right is important --

15 DR. ROTHMAN: Hard to measure.

16 DR. BALZANO: But you can measure it
17 though. That is the point. With the dose phone, all
18 these questions. If we are going to have a good study,
19 I don't think you are do without it. It is interesting
20 that epidemiologists, the closest to science and to
21 quantum mechanics, both of them use observation and
22 statistics. Quantum mechanics uses one more thing -- a
23 lot of population and the dose phone is very accurate.
24 I understand for epidemiology, you cannot have that
25 accuracy and you cannot match that many members of the

1 population, but we should try to get as close as
2 possible to the data that is as accurate as is
3 statistically possible -- not perfect but meaningful.
4 Because all you want to extract is the parameter of the
5 surrogates, but the surrogates should be real good
6 ones.

7 DR. ROTHMAN: Since you brought it up, I
8 think it's worth pointing out how important laterality
9 is. The main problem with laterality is that people
10 are not always consistent. They tend to use the phone
11 in different hands at different times. But there are
12 some people who are consistent and even if that is a
13 comparatively small sub-set of the set of people who
14 are heavy phones users, there is a tremendous amount of
15 information there, because should there be a biological
16 effect, should there be an observed increase, it won't
17 make any sense biologically unless the laterality of
18 the tumors corresponds to the laterality of use among
19 those who are consistently using on one side rather
20 than on the other.

21 And if you have people who are both left
22 sided telephone users and right sided telephone users
23 and you can compare that to the laterality of the
24 organs that are affected with brain tumor -- let's
25 suppose it's brain tumor -- you have a very, very

1 powerful test of a biological hypothesis, even in the
2 face of considerable uncertainty with regard to any
3 other exposure assessment.

4 DR. BALZANO: If I could make one final
5 observation, since this is the antenna, this antenna is
6 not as important as behavior. You talk this way, you
7 get exposure. If you talk this way, you get a
8 completely different exposure. That is essentially
9 what I am saying, but I just want to give you a real
10 clear image of what you are dealing with.

11 DR. MOULDER: Well, it's conceivable that
12 after doing a proper dose phone study, you might end up
13 saying there is nothing which is predictive of what
14 people's actual exposure is. That it is simply too
15 variable.

16 DR. BALZANO: That would be already a
17 pretty conclusion. You can say, in terms -- all the
18 moments are the same, it doesn't matter. Just look at
19 the time of exposure, variability of exposure against
20 an average of exposures in various environment and you
21 are done.

22 DR. ROTHMAN: And laterality.

23 DR. BALZANO: Yes, and laterality.

24 DR. ROTHMAN: Because the dose on one side
25 would be what, two orders of magnitude --

1 DR. MOULDER: More like three or four.

2 DR. ROTHMAN: Three or four.

3 DR. BALZANO: The point is that then you
4 get rid of all these questions.

5 DR. MOULDER: The idea would be you have
6 to do the dose phone study before you design the
7 cohort, before you know what questions to ask on the
8 cohort study. There is no point asking people what
9 model of phone they use if the dose phone study says it
10 doesn't matter compared to the distance from the base
11 station.

12 DR. BALZANO: You might want to start with
13 the dose and then do the other. You can form this dose
14 phone type of assessment after six months to begin with
15 and then periodically, you want to do it again.

16 DR. BASSEN: Is the dose phone though
17 measuring dose or exposures because it's measuring net
18 power?

19 DR. BALZANO: It's measuring net power.

20 DR. BASSEN: So, that only tells you how
21 much power is going into the entire head. If you tilt
22 it, what is the effect?

23 DR. BALZANO: No, no, there is more to it.
24 Also, it has a proximity capacitor that tells you which
25 way is left and right.

1 DR. BASSEN: So, it's more that just total
2 power absorbed.

3 DR. BALZANO: Not power out of the
4 antenna. It's more than that, more than just power out
5 of the antenna.

6 DR. McBRIDE: I was just going to comment
7 that is in a lot of ways similar to the exposure
8 assessment issues we went through for power frequency
9 EMF -- the variability of the source as well as
10 personal characteristics of exposure made it impossible
11 to use those within an epidemiology study for analysis.
12 And, Peter, you already referred to the other problems.
13 If we are able to be precise -- or think we are precise
14 about exposure and where it is, can we be precise about
15 the location of the tumor, the outcome, the
16 relationship of the two.

17 But I would also agree that such
18 characterization studies are useful in identifying high
19 -- in a broad sense, high exposure, low exposure
20 situations and if we can identify those main factors in
21 those situations, perhaps we can use that in some sort
22 of a dose way.

23 DR. BALZANO: Indeed the way to run
24 whatever you want to run, is to just extract good
25 statistical parameters to figure out if some of the

1 exposure (inaudible) truly do make sense or not. You
2 can come up with a tableau that really makes sense.

3 DR. RINSKY: Do we already know if
4 handedness has anything to do with which side you use
5 your phone on?

6 DR. ROTHMAN: Yes, there is very little
7 correlation between handedness and phone use, yes.

8 DR. INSKIP: Certainly, we observed the
9 same thing you reported in your paper and it was
10 actually very counter-intuitive. I expected them to be
11 much more correlated.

12 DR. ROTHMAN: Me, too.

13 DR. INSKIP: For me, I right righthanded,
14 hold the phone in my left hand. I thought many people
15 might do it -- keep their writing hand free, but
16 indeed, it's a horrible correlation.

17 DR. OWEN: The ear is getting warm and
18 they need to warm the other ear.

19 DR. BALZANO: Some models, that is correct
20 and some models, not.

21 DR. OWEN: You mean the degree to which
22 the ear is getting heated?

23 DR. BALZANO: That is exactly right. And
24 that could change from phone to phone. Some people
25 just shift the phone differently because their ear gets

1 warmer and they don't like it and they do that totally
2 in an unconscious motion. They don't even think about
3 it.

4 DR. BASSEN: What about hearing acuity?
5 People who have that acuity would favor that ear, so
6 you might be able to ask that question.

7 DR. ROTHMAN: There won't be enough people
8 with that marked a difference in hearing acuity to
9 matter.

10 DR. LOTZ: I was going to say the same
11 thing. There are going to be too few people with a
12 substantial difference from one side to another.

13 DR. INSKIP: For acoustic neuroma on
14 laterality, we actually observed an inverse association
15 between side of tumor and side of phone use. Non-
16 significant. Indeed, if you through the charts for
17 acoustic neuroma patients on of their symptoms is
18 difficulty hearing and talking on the telephone, so you
19 could imagine it could have been a pre-clinical tumor
20 that caused somebody to switch a side.

21 DR. MOULDER: Do brain tumors have any
22 relationship to your righthanded or lefthandedness?
23 Somebody must have looked at that.

24 DR. INSKIP: We are looking at it now and
25 we have a finding, but there is not much of a basis in

1 the literature to compare it to and I would probably be
2 irresponsible to talk about findings before it goes
3 through a review process, but we have looked at it.
4 There does seem to be an association for glioma, but
5 not for angioma or acoustic neuroma. Just a
6 borderline.

7 DR. MOULDER: Which way?

8 DR. INSKIP: Again, this is preliminary
9 analysis, so --

10 DR. OWEN: This is a public meeting and a
11 transcript is being recorded, so --

12 DR. INSKIP: We are looking at that and I
13 have been trying to find much in the literature and
14 it's not out there. I can't say we put it in our
15 questionnaire to look at handedness. It was to look at
16 handedness as a surrogate for possible biased reporting
17 on the laterality of phone use, which we didn't see
18 evidence of.

19 If there was bias related to that, neither
20 we nor Joshua saw evidence of it, but then other
21 considerations came up for laterality. We are looking
22 at it and I have talked to a couple other investigators

23 and unfortunately it hasn't been included in their
24 study.

25 DR. MOULDER: It's not a totally wild

1 thing to ask because other aspects of brain physiology
2 do depend on your handedness. There is no obvious
3 connection, but it's not wildly implausible.

4 DR. INSKIP: In reports of handedness and
5 breast cancer, people have hypothesized it might be
6 related to certain steroid sex hormone concentrations
7 early in development in the brain, which affect one
8 hemisphere being dominant over the other and if it can
9 affect sites outside, it's at least plausible to affect
10 the brain itself.

11 DR. OWEN: That was something -- the
12 humeral effects, indirect effects mediated by the
13 portable molecules, something that came to mind is in
14 terms of, if you are looking at laterality and you
15 don't find something, that doesn't necessarily tell you
16 that there wasn't anything there. It is sort of like
17 the analogy you were using with the retinal ex-ray
18 exposures and the long bone sarcomas.

19 DR. RINSKY: Epidemiologically, how do you
20 accumulate dose given that a person might be using
21 their phone bilaterally equally? Does that -- person
22 only get half the cumulative dose as someone who uses

23 it all the time?

24 DR. ROTHMAN: No, I think the laterality

25 analyses would be separate from the overall analyses.

1 So for overall analyses, you would ignore laterality.
2 But then you would do a specific analysis presuming
3 they found an excess. Because if you didn't, there
4 would be little point to doing it, but you could still
5 do it.

6 But if you found an excess among phone
7 users -- let's suppose, of brain cancers, then you
8 would want to do another analysis where you took
9 intense users who were consistently using the phone on
10 one side or the other and you try to match that up with
11 the side of the tumor and as Russell said, it's isn't
12 guaranteed that you would see the correlation if there
13 was a biological effect, but if you did see one, it
14 would pretty well nail it.

15 DR. RINSKY: That would be pretty
16 definitive. I guess I was thinking that if it's
17 anything other than a linear relationship, if it's
18 exponential or something of that sort, I don't know how
19 you would normalize one person's experience to another.

20 DR. MOULDER: We are assuming as a sub-set
21 that people always use it in their right hand. I think
22 that is what we are assuming -- that we will find

23 within the group people are bilateral with some
24 frequency, but a certain set that are absolutely
25 unilateral --

1 DR. LOTZ: Actually, Ken, your data showed
2 pretty sizable groups in that respect, didn't it?

3 DR. ROTHMAN: There were good sub-sets
4 that were consistent, let's say, at least 80 percent of
5 time on one side.

6 DR. MOULDER: You wouldn't try to anything
7 with the people who were 60/40, 70/30. They just would
8 just be thrown out of that sub-analysis.

9 DR. RINSKY: I guess that is what I was
10 getting at. It would have to be for the purposes of
11 your general analysis as well.

12 DR. ROTHMAN: No, because they are getting
13 exposure.

14 DR. MOULDER: Or else you just say heavy
15 users get more brain cancers than light users.

16 DR. ROTHMAN: If they spread it around and
17 they don't reach the threshold --

18 DR. RINSKY: I wasn't thinking of the
19 threshold as much as let's say an exponential response.

20 DR. ROTHMAN: Well, it's a similar idea
21 then. Well, that is an interesting theory then and you
22 might need to take that into account in some analysis,
23 but most -- I don't know of any study that has done
24 that.

25 DR. RINSKY: I have never seen anything

1 anything on was -- or very much -- was occupational,
2 but with conventional wireless phones as opposed to
3 push to talks or whatever. Is it feasible or possible
4 that you might identify an occupational exposure where
5 people using conventional phones, but using them a lot
6 or using them in a way that gave you more consistent
7 exposure, higher or more consistent exposure?

8 DR. ROTHMAN: Well, Bob Morgan did a paper
9 on Motorola employees --

10 DR. OWEN: No phone data, right?

11 DR. ROTHMAN: I think there was.

12 DR. BALZANO: On the high exposure area,
13 right. Because the high exposure where people were
14 using -- Morgan did a study of power and transmitter.
15 But there is cell phone in there.

16 DR. LOTZ: But, Russell, you are speaking
17 of people who use a wireless phone, but heavily in the
18 course of an occupation or something?

19 DR. OWEN: Yes, and the reason I was
20 thinking that was because when we were talking about,
21 for instance, push to talks, it was sounding like maybe
22 we were have a hard time finding --

23 DR. LOTZ: Yes, the element that relates
24 to that -- Bob and I tried to answer a congressman's
25 inquiry a number of years ago where the request was

1 that people who were involved particularly in that
2 earlier stage -- it might be different now, but in
3 marketing the phones themselves, were using them -- a
4 magnitude of more minutes than the average user.

5 DR. ROTHMAN: The other group I would
6 think of would be real estate brokers.

7 DR. BALZANO: That is exactly right.

8 DR. LOTZ: So, you do have potentially a
9 few occupational groups that might be pretty sizeable
10 in number, who have a much higher -- I don't know what
11 the data might show now. I remember back in about '94
12 when we started this, the industry had data to show
13 that the average customer and Jo-Anne may know more
14 about this --

15 DR. MOULDER: The average use per customer
16 in the United States --

17 MS. BASILE: Two and a half minutes.

18 DR. LOTZ: Isn't that rather old data?

19 DR. MOULDER: I'm sorry, that is per watt.

20 MS. BASILE: That is the average call.

21 Minutes per month? I don't know if we collected on a
22 monthly basis. Just the average length of a call.

23 DR. LOTZ: There was some data to that
24 effect about six or seven years ago that indicated it
25 was less than five minutes a day for the average

1 customer. Again, the calls were also very short, but I
2 think --

3 DR. MOULDER: I'm curious to know how off
4 the cuff you would define a heavy user. Heavy user is
5 10 minutes a day, an hour a day, two hours a day? I
6 have no feeling for that.

7 MS. BASILE: Depending on the battery, it
8 may not last more than 20 minutes a day, which is what
9 just happened to me. I can't make anything more than a
10 20 minute call.

11 DR. BALZANO: We must have the same
12 battery.

13 MS. BASILE: We have some data about that
14 --

15 DR. ROTHMAN: We had data from our study,
16 yes. I don't remember it off the top of my head, but
17 we had a huge distribution and there were a lot of
18 people who hardly ever used it and there were people
19 who were on it 12 hours a day.

20 DR. OWEN: That was going to be my next
21 question. If we can identify these situations, are
22 they likely to be automatically included in a general
23 cohort anyway or would it be required or more efficient
24 to somehow specifically target these people that are in
25 occupations that you would expect them to be higher

1 users?

2 I mean, when you are talking about real
3 estate brokers, there is a lot of them around, so it
4 just occurred to me, well, if you got a sizeable
5 cohort, then there would probably be a fair number of
6 real estate brokers in that cohort.

7 DR. MOULDER: Well, is it legitimate in
8 setting up a study like this when you advertise and try
9 to attract people to target groups that you think are
10 heavy users? Is that fair?

11 DR. ROTHMAN: Is it. The question you
12 have to worry about is -- you could go to the
13 professional association of real estate agents and say
14 we would like to do a study and get your cooperation
15 and they might promote the study and might get a lot of
16 brokers to join. The question is you may not get very
17 many who are in the comparison side, who are light
18 users and non-users, so that you may have an imbalance,
19 with respect to profession.

20 Now, that may not matter and you may be
21 able to find some professions that you think would have
22 comparable risk, but wouldn't be heavily using the

23 phone and get their cooperation, too. It's an idea
24 that ought to be explored, because if you can get the
25 cooperation of sponsoring agencies, you can get much

1 better follow-up and get much better information. It's
2 ordinarily a good idea.

3 DR. MOULDER: I was thinking that you
4 might end up biasing the cohort by having the heavy
5 users be of different occupations, different
6 socioeconomic class or something from the light users.

7 DR. ROTHMAN: That is what I am saying.
8 But there may be some brokers who are not. We still
9 have a question about whether or not that makes them
10 different in other ways.

11 DR. MOULDER: Do brain tumors have a
12 socioeconomic bias? They do? So, we would have to
13 worry profession then.

14 DR. ROTHMAN: If I remember correctly,
15 it's a higher occurrence in the higher socioeconomic
16 groups, so probably real estate brokers would be in the
17 higher risk category, which makes them more attractive
18 as study participants.

19 DR. LOTZ: Russ, along with lines of your
20 question and shifting slightly from this thought
21 pattern, Barb and I were talking a little about the
22 question of perhaps industrial users of RF. I think
23 that is still potentially a population you could try
24 and study, but it's more scattered and we don't have
25 good demographics on who they are and where they are at

1 this point, but there are a lot of these machines out
2 there and we know that the exposures to people who use
3 them are both pretty significant and plenty of time at
4 it. They stay at that job a lot.

5 DR. MOULDER: What sort of machines? Heat
6 sealer type?

7 DR. LOTZ: Heat sealer type machines.
8 There are other -- induction heaters, things like that
9 that sort of operate similarly and use RF in an albeit
10 quite different frequencies of RF, certainly very
11 different exposure patterns. So, that raises the
12 question of whether it's a good -- I don't have any
13 reservation about advocating that it would be good to
14 learn more about the long-term effects of RF.

15 Whether it's good in terms of cell phone
16 considerations, wireless technology, is a different
17 question. Certainly the patterns of exposure are quite
18 different as well as the frequency. I am less
19 concerned about the frequency differences actually and
20 sort of the generalization of the results, as opposed
21 to the parts of the body that are exposed.

22 In our little side discussion a little
23 while ago, we were just realizing that we just don't
24 have good demographic information on where to find them
25 in substantial numbers. I think they may exist in

1 substantial numbers, but gathering them up into a
2 reasonable group is no small task.

3 DR. OWEN: Did I understand you correctly
4 that in general you were thinking that you maybe had
5 less concern with the difference frequencies between
6 the two scenarios, the wireless communications devices
7 versus the industrial machines than you did about the
8 differences in tissue distribution of the dose?

9 DR. LOTZ: That is correct, what I said.
10 And that was going along the lines of what we were
11 talking about, whether the outcomes of looking at brain
12 cancers and even salivary glands and so forth were of
13 greatest interest to the cell phone.

14 Particularly with something like heat
15 sealers, the head is not by any means where the
16 greatest distribution of energy is. It's going to be
17 the torso and the limbs.

18 So, if the tissues that are most strongly
19 exposed is a critical factor, then there is a loss of
20 comparability there and that concerns me I guess a
21 little bit more than whether we are dealing with 27
22 megahertz compared to 800, 900 or even 1,800.

23 DR. MOULDER: But that is offset by the
24 advantage that the exposure is rather long-term.
25 DR. LOTZ: That's right.

1 DR. MOULDER: Large part of the body,
2 fairly high intensity and if you could find the people,
3 the dosimetry probably wouldn't be easy, but wouldn't
4 be terribly hard.

5 DR. LOTZ: That's true. Certainly, I
6 think dosimetry within the same range of accuracy that
7 we ascribe to phones is achievable.

8 DR. OWEN: When you are talking about
9 tissues to look at, two things just came to mind that
10 maybe will spur a little extra discussion. One is that
11 it reminded me some of what Q. was saying about using
12 the technology and that is that, one, if you are
13 looking down the road to if you had to take any kind of
14 measures, the one thing we can do is change which
15 tissue is exposed. That is probably the -- something
16 is going to get exposed as you pointed out. The
17 antenna, the radiating object is going to be somewhere,
18 but you have control over that in terms of phone design
19 and use.

20 The other thing that came to mind was
21 earlier, we were discussing the paucity of laboratory
22 data for informing us on what we should look at in
23 terms of outcomes or end points and some people might
24 cite the lymphoma results from the M-1 mice as being
25 informative.

1 DR. LOTZ: A related thought relative to
2 tissues which may be exposed brings to mind the whole
3 idea of wireless lap-tops. I don't have any idea what
4 -- Howard, I don't know if you know anything about the
5 exposure --

6 DR. MOULDER: For the local area network?

7 DR. LOTZ: Yes.

8 DR. MOULDER: The power output is
9 minuscule on these.

10 DR. LOTZ: I just don't know --

11 DR. MOULDER: For the Apple Airport, I
12 think it's one of milli-watts. Think of it this way,
13 in a typical house, they are good for about 120 feet,
14 which means they can't be very powerful.

15 DR. LOTZ: You are referring to the
16 wireless lap-top or something like --

17 DR. MOULDER: Your lap-top -- there is
18 your lap-top with a built in cell phone and there is
19 the lap top that is equipped to talk to other devices
20 wirelessly. They are both out there. I was referring
21 to the wireless local area network.

22 DR. LOTZ: I guess I was thinking actually
23 maybe a little wider area network, which I have read
24 about --

25 DR. MOULDER: Ricochet is basically a

1 digital cell phone.

2 DR. BALZANO: It can be a cell phone.

3 DR. BASSEN: There are many technologies
4 that are evolving, so it depends on if you want to talk
5 about the state of the art now or a year from now. And
6 is that base station dependent or is -- so then it
7 wouldn't be that much different from a lot of cell
8 phones, which operate at low levels because of
9 proximity.

10 DR. LOTZ: I don't mean to take us astray,
11 but where do the systems for example that are being
12 talked about in terms of being put in like school
13 buildings, say the extra-portables and things like that
14 that are going to transmit to a central computer and
15 things like that, where do they fit in this picture?
16 That is certainly out of the range of the local
17 network.

18 DR. ROTHMAN: I think anything that isn't
19 held right up against the head is going to be an
20 insignificant SAR compared -- as soon as you get a
21 centimeter away, forget it as far as comparing it to --

22 DR. OWEN: Maybe for Howard's benefit
23 because you weren't here, but at one point, I think
24 that Ken this morning was mentioning that if at least
25 you were designing a cohort study, that you could

1 fairly easily add lots of different -- modern
2 technology uses or something like that, but you could
3 capture many or all of these RF exposures from
4 different sources in such a study.

5 DR. ROTHMAN: What I was saying is that it
6 would be desirable to extend the study to cover various
7 technologies to aid recruitment, for one thing. It's
8 always good to have a more diffuse description and set
9 of objectives for the study so that the study subject
10 themselves aren't too keyed into the key hypotheses,
11 which can be a problem in an epidemiologic study.

12 And also, you have the opportunity to
13 study these other exposures in the study and it would
14 be a mistake not to take advantage of it.

15 DR. BALZANO: Wouldn't that confound your
16 --

17 DR. ROTHMAN: Well, it's unlikely that
18 there would be any important confounders in any of the
19 -- confounding requires some strong associations, not
20 only with outcome, but with exposure.

21 But even moderate associations are not
22 strongly enough to lead to important confounding, so

23 it's possible, but it's unlikely. The real reason
24 would be to study the effects of the other groups.

25 DR. OWEN: People need a break?

1 DR. ROTHMAN: At some point.

2 DR. OWEN: Maybe a shorter break right now
3 for about 15 minutes.

4 (Off the record.)

5 DR. OWEN: I have got a new point, a
6 question that might provoke discussions and might not.
7 And that is can anybody give input as to why one should
8 not do a cohort study or should not plan to do a cohort
9 study this year or next year, but wait for five years?

10 DR. BASSEN: What do you mean by that?

11 DR. OWEN: Are there any arguments against
12 doing a study?

13 DR. BASSEN: A study.

14 DR. OWEN: A study -- for instance, say
15 that you thought the exposure assessment aspect of
16 things was so poor that you could do a whole study and
17 it would be worthless because you really didn't know
18 anything about exposure assessment. In that case, you
19 might say, okay, don't start a new cohort study until
20 you have made great strides in exposure assessment.

21 DR. MOULDER: I don't think we have to
22 make great strides in the exposure assessment, but I
23 think that the dose phone type studies that we were
24 talking about have to be done before you can design the
25 questionnaire, because right now, we don't know what

1 information we need from people. We have no idea
2 whether the model of phone makes any difference in
3 practice. We don't know whether where they use the
4 phone makes any difference in practice and there is no
5 point gathering all that information if it turns out
6 not to matter, and if it does matter, it's critical
7 that we have it.

8 DR. ROTHMAN: These are all important
9 issues, but I just want to stress that in comparison
10 with other kinds of epidemiologic exposures, we
11 actually know a lot about, say telephone use, because
12 the people who are using phones know that they are
13 using them at the very least as opposed to for example
14 exposure to electromagnetic fields, where it's a
15 complete unknown. Or ionizing radiation, which is
16 often known.

17 So, the exposure assessment questions that
18 have been raised are real questions and they ought to
19 be looked at, but we shouldn't get discouraged, because
20 this is something that people can actually identify
21 themselves to a large extent. Use patterns are going
22 to be highly informative.

23 Now, to get back to your actual question,
24 which was can you think of a reason not to go ahead and
25 do it, it really depends who you are addressing that

1 question to. I mean, for anyone who is not actually
2 buying the study, I don't think there would be a reason
3 to hesitate. But if you are the one buying the study,
4 then you have to -- if I am not buying the study, then
5 I am happy to encourage it. If I am buying it right
6 now, then the question is is the cost of the study
7 going to be worth what I am going to get out of it.

8 Unfortunately, in this study and in
9 virtually every epidemiologic study, that is an
10 imponderable. We just don't know, because even though
11 we can quantify the costs to within an order of
12 magnitude, which I consider to be damn good, we can't
13 quantify the benefits at all. And that is what you
14 have to weigh against the cost.

15 So, I don't really know if there is a way
16 to answer that question from the point of view of the
17 person who has to buy the study, or the group that has
18 to buy the study.

19 From the point of view of everyone else,
20 yes, do it tomorrow.

21 DR. MOULDER: I think even from the point
22 of view of the person buying the study, this type of
23 cohort study that we discussed is the only one that is
24 really available and informative to do at the moment.

25 The case control we talked about, at best

1 would duplicate what IARC is already doing. The
2 occupational studies we talked about are maybe not even
3 doable. The one other study we talked about is a
4 fairly cheap one and that is monitoring some of the
5 tumor registries to see if incidence is changing with
6 time and that is something you can do anyway.

7 DR. OWEN: Good. Thanks.

8 DR. LOTZ: The one occupational group that
9 we may have kind of skipped over and I don't know if
10 this is even the time to interject it because it's kind
11 of breaking the flow of your question, Russ, but would
12 be military members.

13 There is a lot of tracking of those
14 people. The ones that were done, historically have
15 been done on veterans, a long, long time after, which I
16 think is what has presented a lot of difficulties there
17 with very rough assumptions about jobs and things like
18 that, but there probably are some specialties within
19 the military services that have some regular exposure.

20 There is probably a need for some maybe
21 better exposure assessment on certain types of jobs to
22 get a handle on what is even high, medium and low.

23 I don't know if we have the information to
24 answer the question, but it might have some merit in
25 the context are there any occupational groups out there

1 that you can study.

2 DR. RINSKY: From a public health
3 standpoint, would this study in any way compete with
4 any public health resources that otherwise go to
5 something else? I don't think so. From a funding
6 standpoint, what about FDA? Because there are
7 certainly more important things to work on. Even
8 around cellular phone use, it's almost silly to look at
9 brain cancers in light of what Ken found in automobile
10 fatalities. You do things in a certain order.

11 So, if they were competing with one and
12 other, that would be my only objection.

13 DR. OWEN: And unfortunately, you are
14 right. That is not a situation here just because this
15 is a targeted activity, to stay on target. We already
16 decided that we would be looking at these things, these
17 questions. So, at least not as far as I can tell in
18 direct competition with resources. There is sort of
19 already a decision to commit resources to this area.

20 I'm not trying to say you are committed to
21 doing epidemiologic studies at this time, but the
22 cooperative research project in general.

23 Okay, I was hoping I could rile people up.
24 DR. MOULDER: There was one other part of
25 the question you asked, was there any argument to delay

1 and I think there is a strong argument that says if you
2 are going to do a cohort study, you had better get
3 going, because the quality of information is going to
4 drop steadily with time.

5 The longer you wait to start it, the more
6 retrospective information you have to collect from
7 current users and the weaker that is going to be.

8 DR. OWEN: I had thought we wouldn't be
9 able to get to it this soon, but if you are willing
10 right now, to give us 10 minutes or so --

11 DR. LUNDQUIST: I was just going to say to
12 you I have done something so different from what is
13 going on now, that I can talk very briefly or at length
14 and I think as informally as this group is meeting and
15 as thoroughly as you are trying to discuss all things,
16 it might be better for me to speak at some length
17 rather than trying to abbreviate.

18 What time is it now? About 4:00?

19 DR. OWEN: Yes, I have got 25 until 4:00,
20 but I was thinking it would be helpful if you spoke
21 only as you suggested on the exposure assessment for
22 the purposes of this meeting. So, I thought maybe 10

23 or 15 minutes, if you could just cover that part and
24 then we will have --

25 DR. LUNDQUIST: Are you saying you found

1 what I handed you to be inappropriate for this meeting?

2 DR. OWEN: It's pretty broad-ranging and I
3 would like us to stay directly related to the
4 epidemiology studies since that is the topic for this
5 meeting.

6 DR. LUNDQUIST: Well, all right, but I
7 think everything that I have to say in some way or
8 other references these issues.

9 DR. OWEN: Okay, I'll just keep an eye on
10 the time basically and then we can have discussions.

11 DR. LUNDQUIST: I have prepared an
12 overhead transparency and I have got a hand-out here
13 and I thought maybe the sensible thing for me to do
14 would be just to give you this. Does everybody have a
15 copy?

16 What I did here was try to consider what
17 are the parameters to define the health hazards from
18 use of wireless telephones and I roughly tried to list
19 these in descending order importance in my own
20 estimation.

21 So, the very first one is duration of
22 continuous use and what I mean by that is length of a

23 single conversation or it could be successive
24 conversations following one another very rapidly, with
25 say no more than 10 or so between then. That could all

1 be considered one consecutive continuous exposure.

2 I have come to the conclusion, both as a
3 result of somebody contacting me for help whose health
4 was damaged by long conversations on a digital phone,
5 plus my reviews of the literature saying that the
6 Russians 20, 25 years ago were saying duration of
7 exposure is an extremely important variable.

8 Now, it would be easy and I think most of
9 us tended to think that it was a cumulative duration of
10 use that was important, certainly that is what the
11 billing data from the company record would give you --
12 so many hours per month or something like that.

13 But I think that may be an error. Now, if
14 I can get this overhead to work -- what I have done
15 here is to sketch a situation where you might a
16 population of individuals, but if you were doing say a
17 primate study, you could actually do it a population
18 where say, one is holding six-minute conversations and
19 the other is holding 60-minute conversations. The
20 factor of 10 difference is the duration of the
21 continuous exposure. But we are saying they have the
22 same total time of exposure.

1 DR. LUNDQUIST: This is like a frequency
2 histogram. In other words, total time. I'm just
3 saying it the same total time.

4 DR. BASSEN: But are you saying that an
5 individual who is speaking for six minutes and
6 listening for --

7 DR. LUNDQUIST: No, no. I mean, usually
8 in conversations there is a fairly frequent
9 interchange, so I am saying basically you are live on
10 the phone for six minutes. Maybe you are talking the
11 whole time, if you want to start getting technical
12 about the difference between when it's transmitting and
13 when it's receiving, because that is important.

14 DR. BASSEN: But aren't these always
15 transmitted at the same level whether you are speaking
16 or --

17 DR. BALZANO: The phone when it is on,
18 unless it has a voice --

19 DR. ROTHMAN: I think the point of the
20 question is whether or not in total time, it's divided
21 up into one-hour blocks or is it six-minute blocks.

22 DR. BASSEN: The total time of the --

23 DR. ROTHMAN: Of use of the phone.
24 DR. LUNDQUIST: Yes, the phone rings and
25 you answer it or you dial out and you spend six minutes

1 conversing with somebody and then you hang up. You
2 have had a six-minute conversation with somebody versus
3 a 60-minute one.

4 The reason I came up with something like
5 60 minutes is because this guy, who was very clearly
6 injured, I examined his reported health problems very
7 carefully, looked in the literature and there seemed no
8 question that this was microwave damage. It's
9 documented in the literature, the kind of damage he
10 had, as occurring in other people. There was no
11 question of microwave radiation damage.

12 He said he was holding more than hour-long
13 conversations with his cellular phone with his wife
14 because of domestic problems. He was a trucker on the
15 road. So, he was having multiple long conversations in
16 excess of 60 minutes. That is where you see your
17 problems develop severely and rapidly. That is the
18 kind of population to look at if you want to see health
19 effects quickly and severe effects.

20 But the point I was trying to make is even
21 if the total amount of time -- as I say you can set
22 this up in say a monkey population or something
23 artificially exposed with cellular phones strapped to
24 their heads or something, where you could control the
25 total time and then control what kind of length of

1 intervals it is divided into.

2 If you did this kind of study, and I am
3 saying held constant the total time, so that maybe one
4 60-minute exposure versus 10 six-minute exposure, say
5 an hour apart or something like that, I am saying that
6 if you made the assumption is that the total time is
7 what is really relevant here, I think you would come up
8 with results that don't make any sense, but that wasn't
9 really the variable that was the critical one.

10 To put it another way, I am just saying in
11 this lower one that there is a risk associated with the
12 duration of a single conversation. You could say a
13 linear function if you want to quantify this, although
14 probably it isn't linear. It's probably something that
15 might be exponential or if there is a saturation
16 effect, it might turn into an S curve or something like
17 that.

18 But the obvious simplest approximation to
19 make on the first attempt is a linear waving function,
20 where you would try to look at these long
21 conversations, especially because they are the most
22 risky or the most hazardous. And in this context, by

23 the way, I think the idea of looking at occupational
24 groups such as real estate sales people who do tend to
25 use a phone pretty heavily while they are driving,

1 because that is the only time they have a chance to use
2 it probably, might make very good sense, but you are
3 going to have to get some information about the
4 distribution and length of these calls so that you can
5 look at the long ones and see who has been having long
6 calls and whose hasn't.

7 Back to the handout, whether the phone
8 used emits an analog signal or a digital signal in my
9 view is an extremely important variable. It's because
10 I believe it controls the health effects that you are
11 going to see at least early on.

12 So, categorizing is important in terms of
13 categorizing people in terms of whether they used an
14 analog or digital phone. You could make subdivisions
15 of the digital -- I have no idea at the present time
16 whether those subdivisions are important or not, but if
17 you are doing a big study and you can make those
18 subdivisions, then maybe you can get some information
19 about whether they are critical.

20 Now, I split this up for analog and
21 digital phones because, as I said, the health effects
22 could be quite different. With analog phones, I think

23 it's possible to see brain cancer as a health effect in
24 those people who have had these long conversations,
25 long periods of uninterrupted use, continuous use,

1 however you want to characterize it.

2 And in fact, I think if you look at these
3 lawsuits that have been filed and if you can get
4 information about the pattern of use of the phone of
5 each of those individuals who were affected, I think
6 you are going to find exactly that. And that might be
7 worth doing.

8 Of course, as Dr. Rothman pointed out, you
9 have got to have people consistently using the phone is
10 the same side of the head or you are not going to have
11 the same risk of showing tumor.

12 The frequency of radiation is going to be
13 a variable of concern. The analog phones, I think use
14 in the US two different frequencies -- or maybe there
15 is only one -- but, at any rate, the analog phones tend
16 to have their frequencies contained within a relatively
17 narrow band. It's probably not narrow in an absolute
18 sense, but relatively narrow. The digital phones
19 spread it out over a very wide frequency range and the
20 power tends to be lower in each frequency increment as
21 a consequence, so you have both a difference in the
22 spread of frequencies that the person would be
23 subjected to and in the power at each frequency.

24 Obviously, total use cumulative is a
25 variable that has some value and the radiated power

1 from the antenna probably is a variable that also has
2 some import, although I am not sure that it's terribly
3 important. However, for the analog phones, I am
4 suspicious that low power may be more hazardous than
5 high power and now I would like to show you why.

6 The usual assumption that we make when we
7 are thinking exposure and dose is that higher radiation
8 power densities are more harmful for thermal exposures
9 or for thermal effects. This is certainly true. All
10 the thinking that has led to our setting of standards
11 and everything has been based on the thermal model.

12 However, when it comes down to the non-
13 thermal, I am not at all sure that that is so true.
14 This is in the chapter four publication, which you will
15 find on the back the fourth page of the handout, the
16 citation for that. There is experimental evidence,
17 some experimental evidence to suggest that instead of
18 this being a straight line monotonically increasing or
19 any kind of monotonically increasing curves, we may
20 have something like a bell-shaped curve where you have
21 a region of hazard flanked at lower and higher levels
22 with regions of reduced hazards.

23 DR. OWEN: Excuse me. I am having trouble
24 seeing how this relates to our discussion of
25 identifying gaps in epidemiologic studies or exposure

1 assessment in particular.

2 DR. LUNDQUIST: Well, Howard was talking
3 about exposure and dose, so I thought it was relevant.
4 In that context it is, because if all the assumptions
5 are based on this and the reality is that, you got a
6 problem coming down the pike.

7 I am about to wind up and I will just say
8 that while I don't have any theories that would explain
9 this kind of relationship in a fundamental sense, the
10 stochastic resonance will explain it functionally I
11 think and I can tell you who has some information if
12 you want to follow up on that, but I am not going to
13 talk about that any more now.

14 But I do think the issues of exposure and
15 dose are important. That is why I brought that up.

16 Back to the printed thing. We will talk
17 about digital phones. Here, it looks to me like
18 problems that are going to show up earliest are going
19 to be with memory, particularly with what we say is
20 short term memory, although actually if you get down
21 into it in a physiological sense, I really think the
22 problem isn't that something is wrong with short term
23 memory. Something is wrong with turning short memory
24 into long term memory. That doesn't happen and then
25 you lose what you were able to remember for a short

1 time because you weren't able to transfer it to long-
2 term memory. But it is usually described as a short
3 term memory problem.

4 Again, that will show up, I think, in the
5 people who had these long uninterrupted exposures, the
6 long continuous exposures.

7 Persistent unclear vision in one eye, I
8 have thrown that in because of this guy, who I told you
9 about had the hour-long conversations with his wife
10 when he was driving the truck using a digital phone,
11 because one of his problems with the eye on the side
12 where he used the phone.

13 Persistent unclear vision, that problem is
14 documented in microwave exposure in the medical
15 literature and after careful study of the literature, I
16 have concluded that almost certainly, this man has
17 destroyed the corneal endothelium in the affected eye.
18 The corneal endothelium controls the thickness of the
19 cornea, which controls the major amount of refraction
20 of light entering the eye. This persistent unclear
21 vision, I tended to call it fuzzy vision, but that
22 might not be appropriate -- I don't know. I
23 distinguish it from blurred vision where you get your
24 image focused in front or behind the retina. There
25 have been studies done in monkeys with microwave

1 radiation that show that microwave radiation can and
2 will damage the corneal endothelium and I think that is
3 what has happened to these microwaved individuals and I
4 think that was has happened to this man.

5 The way to test it -- and he wanted to be
6 a research subject now, he is looking for somebody
7 willing to spend some money to learn from what happened
8 to him, so it won't happen to other people, so if
9 anybody who knows anybody who wants to spend some money
10 studying damaged individuals to find out more about
11 what happened to him, please let me know because he
12 would love to have that happen before he ends up dead.

13 DR. OWEN: I think we are outside the
14 scope of our discussion now.

15 DR. LUNDQUIST: Yes, but I wanted to
16 suggest in terms of epidemiologic studies that you
17 might want to consider this as a health affect to look
18 for.

19 DR. OWEN: Right.

20 DR. LUNDQUIST: And since we are speaking
21 of eyes at the moment, let me mention that I am very
22 suspicious of macular degeneration. I don't have any
23 evidence that convinces me this is happening, but I am
24 suspicious that macular degeneration could be another
25 affect on the eye on the side of the head people are

1 consistently using -- well, I don't know whether it
2 would be digital or analog, so you would have to look
3 at both -- in terms of something that would happen.
4 But the incidence of macular degeneration in the
5 youthful section of the population or at least the
6 middle-age section, is rising, so the age at which
7 people are affected is dropping and they have no
8 explanation for that.

9 Back to the digital phones, the radiated
10 power here, I suspect the higher power here may be more
11 hazardous than the lower power. The frequency of
12 radiation is important certainly and of course when the
13 user consistently uses the phone on the same side of
14 the head.

15 I'll turn now to the next page. Really,
16 other than just reading this, there isn't whole lot of
17 point to going through it in detail unless there is
18 some discussion that you want to talk about.

19 The point I want to make, I will just make
20 extemporaneously. The existing exposure metric is the
21 power density and that is the magnitude of Poynting
22 vector. This is appropriate for plane wave. In the
23 publication, chapter four, that is referenced on the
24 back, that is presented mathematically in clear detail.
25 I think practically anybody who knows math can follow

1 it.

2 However, as soon as you start getting into
3 something that is not a plane wave, you start running
4 into a different situation where it's not at all clear
5 that that is a valid exposure metric.

6 Again, that chapter four goes into --
7 presents equations, which have not been taken far
8 enough along that I can tell you what would be a useful
9 exposure metric to use for non-thermal effects, but we
10 have two different exposure metrics. One for thermal
11 effects and one for non-thermal. They are different
12 exposure mechanisms and the mathematical equations are
13 different. Again, I refer you to that chapter four.

14 I say here in one of these paragraphs at
15 present, the best way to take these parameters into
16 effect is to categorize the population under study very
17 thoroughly and in considerable detail.

18 I'm in 100 percent agreement with Dr.
19 Rothman when he says if you take a carefully chosen
20 small population and look at it and get some useful
21 results, that is a very powerful result and I think you
22 can get a lot more bang for your buck if you do very
23 wise choice of very carefully selected small
24 populations and then examine them very thoroughly.

25 DR. OWEN: I want to move on now.

1 DR. LUNDQUIST: Okay. I think the near
2 field of a radiation sources has sufficient parameters
3 in common with the field outside a hollow microwave
4 waveguide that they can be considered to be in the same
5 category if you are categorizing things. I will point
6 out that exposure to something within the fields inside
7 a waveguide is typically an accidental exposure and is
8 usually regarded as some kind of emergency. When we
9 expose people to the near field of a cellular phone,
10 it's not considered an accident and yet, I think the
11 health effects are the same.

12 DR. OWEN: Before we move on to the rest
13 of the day's discussion, I want to make sure and ask
14 anybody if they have questions or comments on what Dr.
15 Lundquist has shared with us.

16 DR. LUNDQUIST: I have categorized some of
17 the health effects here on the back page. Non-thermal
18 ones include cancer, memory problems, persistent
19 anxiety, post traumatic stress syndrome, destruction of
20 corneal endothelium and pain. The thermal health
21 effects are the sensation of heat.

22 I give two examples up here about pairing

23 up the exposure metric and the health effect and I will
24 remind you that SAR is a thermal measure of exposure.
25 The other stuff, probably is too technical for anybody.

1 Since you wanted me to do it quickly, I'm
2 done.

3 DR. OWEN: Thank you. Any questions or
4 comments on that material?

5 DR. SLESSEN: I would like to ask the
6 panel a question, if I may at this point.

7 DR. OWEN: Briefly.

8 DR. SLESSEN: I would like to hear why the
9 United States is not involved in the IARC study and any
10 comments you would have on whether there would be some
11 involvement at some point. It just seems like there
12 are 13 countries and the United States is not among
13 them and given that some principles are here and we are
14 talking about epidemiology --

15 DR. OWEN: That is probably not a question
16 people would want to answer in this forum, but I am
17 sure that people would be happy to talk to you
18 immediately after the meeting -- or not.

19 DR. SLESSEN: I think it's germane if you
20 were talking about doing epidemiologic research, why we
21 are not part of that as a country. I think it is
22 germane to --

23 DR. ROTHMAN: Shouldn't you address that
24 to IARC?

25 AUDIENCE MEMBER: This is a US government

1 panel --

2 DR. OWEN: No, this is not a panel and
3 it's not just the government.

4 AUDIENCE MEMBER: I mean, there may be
5 very legitimate reasons. I have not heard why we are
6 not participating.

7 DR. ROTHMAN: I think we would just be
8 speculating.

9 AUDIENCE MEMBER: I don't want
10 speculation. I mean, somebody with primary knowledge.
11 Not speculation, but I would think that maybe Dr.
12 Inskip has been approached at some point --

13 DR. OWEN: Again, I think it's outside the
14 scope of the scientific discussions here. I recognize
15 that it's a worthwhile question and that some of the
16 people here may be able to provide answers on that, but
17 I don't think it belongs in the conduct of the meeting
18 itself. I thought you were going to focus on a
19 scientific question.

20 So, anyway, you know what Dr. Slessen
21 wants to talk to you about if you have time to talk to
22 him after the meeting. And I anticipate that we may
23 get done early.

24 What I have planned, as you know, is that
25 we have a little bit of time tomorrow morning. We

1 should be able to start -- I think it's reasonable to
2 wait until 8:30 to start tomorrow. Some people of
3 course won't still be here then and I am not sure how
4 many people will be here then. And certainly, we can
5 expect to be done before 11:00 tomorrow morning for
6 anybody who is still around.

7 What I will try and do tomorrow morning is
8 start off by sort of giving a brief review of some of
9 the input that I have heard today as a way of seeking a
10 little bit of clarification or refinement on what we
11 have already put on the table.

12 DR. ROTHMAN: Since people are going to be
13 leaving anyway and since we are talking about wrapping
14 up early this afternoon and having a shortened day
15 tomorrow, is it out of the question to try and consider
16 moving tomorrow to this afternoon and try and wrap the
17 meeting up today?

18 DR. OWEN: We could try and do that except
19 that doesn't give me any time --

20 DR. ROTHMAN: We could sit around the
21 table and help you and circulate your written opinion
22 later when --

23 DR. OWEN: Okay, before -- I would like to
24 try and do that, but before we do that, I wanted to
25 solicit areas of discussion that we haven't touched at

1 all before we go back and intentionally rehash areas
2 that we have already dealt with.

3 So, I just wanted people to pause a moment
4 and think if there are other areas that are critical to
5 identifying knowledge gaps in the epidemiological
6 studies and then the types of studies that could
7 address those gaps.

8 DR. LOTZ: I think I would bring up one
9 point and, actually Dr. Lundquist kind of focused on
10 this to some extent, but we touched on it earlier, but
11 I don't know that we really reached much considered
12 thought on it and that was whether or not there was a
13 need to try an epidemiological study the more acute --
14 I don't know if I should call them acute, but the non-
15 cancer, more neurologic end points like headache,
16 memory loss, things like that that are -- I refer to
17 them as more -- not necessarily that they are in a
18 single exposure, but they are more short term, I guess
19 would be a better term to use for them.

20 I don't really see them as fitting the
21 design of a long term cohort study unless they were a
22 superimposed element on that because I think they
23 involve a completely different set of outcomes, so my
24 question is is that an area that we need to address
25 with epidemiologic studies at this point in time?

1 DR. MOULDER: I have got a question for
2 your question.

3 DR. LOTZ: Yes.

4 DR. MOULDER: I don't understand why it
5 would be so difficult to add those to a cohort study.

6 DR. LOTZ: Well, I may be wrong that it
7 is. I just think it's a focus on a different set of
8 outcomes with a different time interval of onset. So,
9 I think at least in the early going, I think you need
10 to have information from people on a much more rapid --
11 frequent basis. You couldn't set up an initial start
12 and wait to go back to them six months later I don't
13 think and I think you may have to focus more on even
14 perhaps new users.

15 So, I am not sure. But I am thinking that
16 there are some different parameters there that would
17 appreciably affect how you conducted that part of the
18 study, not to mention the very difficult nature of
19 characterizing those outcomes anyway.

20 But I wanted to come back and address that
21 question, because it does come up in -- for those of us
22 in agencies, we get calls somewhat like the case that
23 was just described by Dr. Lundquist where there are
24 individual cases that they keep raising this issue.

25 It's the issue that was raised enough to

1 cause the Swedes and the Norwegians to undertake a
2 major study of 12,000 people to specifically try and go
3 after those kinds of things. It's an unanswered health
4 question about the use of these technologies that may
5 or may not be amenable to study.

6 DR. OWEN: Actually, you mentioned the
7 Swedish headache study, I guess that is a good place to
8 move the conversation forward in terms of what is left
9 as a data gap from that study. Obviously it was only
10 looking at some of the non-specific subjective --

11 DR. LOTZ: I think part of the data gap
12 there is just simply that it's an initial exploratory
13 study. The interesting finding so far at least is that
14 the incidence of the self-reported outcomes, headache
15 and a few others, was well-correlated with the amount
16 of use of the phone -- I believe characterized in the
17 number of minutes per day.

18 They I think are in the process of
19 continuing to do studies to try and look -- their
20 initial hypothesis was that it would be more associated
21 with digital phone use rather than analog and that did
22 not hold up. That hypothesis was not supported by
23 those findings, which I think is a very meaningful
24 outcome of that study and in fact was the -- the design
25 was intended to try and get at that question.

1 DR. MOULDER: That does bring up a weak
2 point in the study. It's a comparison of analog users
3 to digital users. There is no non-user cohort in it.

4 DR. LOTZ: Well, in the context of our
5 discussions earlier today, there was a component or
6 stratification of a exposure, so there was a group that
7 had very low use. Like less than three minutes per
8 day.

9 DR. MOULDER: I didn't realize that.

10 DR. LOTZ: So, there is some
11 stratification that way, but you are absolutely right.
12 The design of the study was to say let's compare analog
13 to digital and see if there is a difference in these
14 outcomes compared to that and there was not.

15 DR. McBRIDE: I would think that the
16 design was such that that kind of study would be
17 sufficiently different from that of a cohort, the study
18 that we talked about, that they may have to be
19 separate.

20 If one is going to look at outcomes, short
21 term outcomes such as headache, first of all, there is
22 the consideration of the other factors that might be
23 involved in causing that outcome. And Ken's remarks
24 about knowing the subject of the conversation, is
25 probably relevant there.

1 The definition of an outcome such as
2 headache is problematic and lastly the validity of
3 self-reports for many of these is problematic. Self-
4 reports are probably not adequate, particularly one can
5 see that there is a huge potential for bias in
6 reporting these kind of symptoms.

7 And last, it comes up where there is the
8 subject of the conversation or some other aspect of
9 using the phone, whether it's the strain of holding the
10 phone to the ear or, as you pointed out, Q., the fact
11 that your ear gets warm and you tend to put yourself in
12 a certain physical position to use the phone for long
13 periods of time.

14 How do you separate those factors of phone
15 use from the radiation? I have trouble thinking of a
16 sham, in a sense, instrument that would duplicate all
17 of those factors, that would seem like a phone, but
18 didn't have radiation.

19 DR. MOULDER: If you did want to study
20 headaches, since the idea there is that the immediate
21 use of the phone causes it, you are really describing a
22 human experimental study, rather than an
23 epidemiological study.

24 DR. McBRIDE: That is a good point.

25 DR. MOULDER: And with a little

1 technological wizardry, somebody probably could develop
2 something that looked -- for a lab, that looked like a
3 cell phone and acted like the a cell phone, but did not
4 produce RFs. You could figure out some other way to
5 get the sound to it. You could wire up both of them.

6 DR. McBRIDE: Yes, you are right.

7 DR. LOTZ: I guess the gap as I see it is
8 not a single laboratory session type experiment,
9 because I think there have been a number of those that
10 have tried to determine even taking subjects who were
11 self-reported coming in as electro-sensitive, and
12 trying to determine in a blinded manner whether they
13 could identify the symptoms as indicative as the
14 presence of the field and strangely enough, they have
15 not been able to even though they were persons who
16 reported sensitivity to these kinds of problems.

17 The gap that I see is whether that kind of
18 exposure over a number of days or weeks, yet in a short
19 term, somehow contributes to the development of such
20 symptoms. And kind of regardless of whether I think it
21 will or will not, I think there is that kind of a need
22 in the public health arena to answer that question.
23 Whether a study can be designed to do that or not, it a
24 different matter, but I think that question is out
25 there.

1 DR. LUNDQUIST: The comment on the
2 sensitive people not responding in the laboratory, I
3 did read that literature, but it's been some months
4 back and it's not fresh in my mind. My recollection is
5 that when the people reporting that they didn't respond
6 to the field in the labs, they were exposing them to
7 extremely low frequency fields primarily -- not radio
8 frequencies.

9 DR. LOTZ: There are a number of newer
10 studies in the last couple of years that have used RF.
11 That's what caused me to make that statement.

12 DR.LUNDQUIST: The other thing is that the
13 response maybe to a radio frequency field that is a
14 characteristic of inefficient antenna. There is good
15 reason to believe that the health effects of that will
16 be much worse than the radio frequency field
17 characteristics of an efficient antenna.

18 DR. OWEN: I guess another thing that
19 might be difficult to assess at this point is what
20 other studies soon may begin that might address that
21 need, given the program that is just getting off the
22 ground in the UK or at least the establishment of
23 funding and rumor that it will be focused on certain
24 types of end points, but that is not yet determined.

25 DR. LOTZ: There was a segment of the

1 perform agenda that was going to address that, but then
2 that segment was not pursued; is that correct?

3 DR. BALZANO: I think it is going to be
4 funded.

5 DR. LOTZ: They are coming back to a point
6 of funding it?

7 DR. BALZANO: I think so.

8 MS. BASILE: I think they are thinking
9 about it. I was just talking to Louis about this
10 earlier. I don't know where I saw this. Did people
11 get the newsletter this week? Is there a solicitation
12 for proposals from the Stewart group?

13 DR. MOULDER: I don't think it's formal,
14 but it described the solicitation from the British
15 government. And headache and memory are two of the
16 things in that.

17 MS. BASILE: There is a series of
18 epidemiology studies focusing in on children and
19 subjective health symptoms.

20 DR. MOULDER: They are saying we are
21 soliciting proposals in this area. I don't think we
22 will know for months what they get and what they fund.

23 DR. OWEN: Yes, I recently spoke to
24 somebody who is on the scientific advisory committee
25 for that set of studies and at the time that I spoke to

1 them, they hadn't even met yet.

2 DR. MOULDER: So, there may be studies in
3 this area and there may not have. I don't think we
4 will know for six or eight months. We could find out
5 what World Health Organization is planning on doing in
6 this area, but I think most of the research in this
7 area has been Swedish and German.

8 DR. LOTZ: Yes, I think that is correct.
9 I just happened to pick it up in my mailbox this
10 morning -- bids are particularly invited in the
11 following areas -- this is from the Stewart Commission
12 -- effects on brain function, consequences of exposure
13 to pulse signals, improvements in dosimetry, sub-
14 cellular and cellular changes induced by RF and their
15 possible impact on health, psychological and
16 sociological studies related to the use of mobile
17 phones and epidemiologic and human volunteer studies
18 including the study of children and individuals who
19 might be more susceptible to RF radiation.

20 DR. OWEN: Anybody want to add anything
21 else at the moment on that topic?

22 MS. BASILE: Russ, while you are compiling
23 a list of studies, I understand that Leonard Tarbell
24 (phonetic) is planning on making a public presentation
25 in June about some further work that he has done on --

1 expansion from his original pilot study.

2 DR. INSKIP: This is beyond the re-
3 analysis they published in Muscat, so actually more
4 cases and controls.

5 MS. BASILE: Many more cases.

6 DR. OWEN: Any other additional separate
7 sort of topic areas that we haven't touched on that
8 comes to people's minds?

9 I will try to dive in per your
10 recommendation. Well, the easiest -- I will sort of
11 start where we started and that was mostly with case
12 control and I tried to put it as short as possible.
13 What I heard was nobody making a case for additional US
14 case control studies similar to the studies that have
15 recently been published in the near term.

16 DR. MOULDER: And furthermore, no reason
17 to parallel the studies that are starting now.

18 DR. OWEN: There was some discussion of
19 other case control, some other case control studies,
20 but I didn't -- at the moment, I didn't get the feeling
21 that there was input to the effect that there was a
22 compelling need or a priority for these other

23 approaches compared to the widely discussed benefits of
24 a cohort study, so the overriding thing that I have
25 heard is that there is a lot of support for doing a

1 cohort study and perhaps that is the only thing that we
2 can really do right now that would be of a real benefit
3 as it could be conducted now, assuming that it's
4 properly informed by dosimetry-related sub-studies and
5 for both it's sort of continuing validation during the
6 conduct of the study as well as input into the design
7 phase for questionnaires.

8 So, that is in the rawest terms I can
9 think of mostly what I have heard today. If people
10 want to nail that down a little further, maybe
11 highlight points that were made earlier.

12 DR. ROTHMAN: Just in the nature of
13 summary, I have a list of a few of the reasons why I
14 think a prospective cohort study would be the study to
15 consider.

16 While we haven't talked about it, implicit
17 in much of the discussion that I heard is that we are
18 not just talking about the cohort study. We are
19 talking about a prospective cohort study here. It's
20 pretty obvious in the context, but it's worth
21 emphasizing the description.

22 So, why would we want to do a prospective
23 cohort study and here is my list of reasons. It's not
24 necessarily complete, but number one, we need to
25 characterize the exposure prospectively rather than

1 interview people after they have had brain cancer, for
2 example.

3 Number two, we need to characterize the
4 exposure periodically as well, so that we can see how
5 it changes over time.

6 Number three, we need to study many
7 different outcomes.

8 Number four, we are interested in studying
9 an effect that could occur after a very long induction
10 time. Though it is possible to study long induction
11 times in case control studies, it's very difficult when
12 you are talking about accurate exposure
13 characterizations. So, unless you start with that and
14 work your way forward, you can't do it very well.

15 The fifth reason I have is that it's
16 possible with a prospective cohort study to invite into
17 the study people who specifically have high exposures.
18 In a case control study, you take what you get pretty
19 much. This way, you can focus on those you think are
20 the most interesting to study, as in example as came up
21 in the discussion the possibility of inviting realtors
22 as a occupational group to study in this way.

23 So, that is my list of reasons and maybe
24 others can add to it, but those reasons, each of them I
25 think would be sufficient to warrant a prospective

1 cohort study and together they make a very strong case.

2 DR. MOULDER: I think another thing worth
3 specifically mentioning is the idea that the study
4 would be web based for follow-up and possibly even for
5 recruitment.

6 DR. ROTHMAN: I have another list of the
7 features of the study, which I was saving.

8 DR. MOULDER: Is it really correct to call
9 this -- this is a retrospective as well as a
10 prospective cohort study if you would be following
11 people's exposures in time after day zero, but also
12 looking back to see what their exposures were before
13 day zero?

14 DR. ROTHMAN: It's a good question and the
15 answer is a little complicated because different
16 epidemiologists use different definitions of what is
17 retrospective and what is prospective. One definition
18 and the one that I have usually used, but it's by no
19 means universal, is that what makes a study prospective
20 is that the events that you are study occur after you
21 begin the study. But not everybody uses that as the
22 definition.

23 If you can use that definition, then even
24 with the retrospective information on exposure history
25 at the start, it's still a prospective cohort study.

1 DR. OWEN: You want to talk about
2 features?

3 DR. ROTHMAN: I have a list of features,
4 which again is not a complete list and a lot of it
5 would need to be second guessed, I think, with a little
6 more careful thought and they are not in order of
7 importance either. Number one, I wrote, that we are
8 talking about -- my guess -- is approximately 50,000
9 people, who would be followed for at least 10 and maybe
10 up to 20 years or so, so this is a sizable cohort study
11 and followed for a long time, but not as big as they
12 get. The nurse's health study has been going already
13 25 years, so they go longer and they are much bigger,
14 too.

15 Number two, we would want to recruit
16 people and get very detailed baseline information.
17 People who aren't willing to give it, they wouldn't be
18 included in the cohort and that would be one way of
19 focusing on those who are eager participants, which is
20 important for ultimate follow-up.

21 So, we get detailed baseline information
22 not only on the exposures of interest, but on all sorts
23 of other variables that would be important to have.

24 Third, we would use some scheme for
25 periodic exposure assessment and periodic inquiries

1 about potential outcomes. A convenient way to do this
2 that we talked about would be web based access to this
3 information. For outcome inquiries, what you do is you
4 ask people have you been ill, have you been
5 hospitalized, have you had any of the following
6 conditions and then only if they say yes do you get
7 more information, otherwise you just leave it as a
8 screen.

9 We already talked about the kinds of
10 exposure assessment information that we would get
11 periodically. We said something like six-month
12 intervals would probably be a good idea.

13 Another feature would be that I think it
14 would make sense to include not just exposure to
15 cellular telephones, but other exposures that we could
16 conveniently study and one way to package it might be a
17 study of exposures to modern technology. You can think
18 of several that might be included. That would defuse
19 the focus a little on cellular telephones, which helps
20 the validity of the study and might help you recruit
21 the right range of subjects and might help comparisons
22 that we might make. In addition, it enables us to
23 study the effects of other factors as well.

24 One thing that I think is very important
25 is that in the recruitment of this study, you want to

1 go easy on recruitment. You don't want to use
2 incentives. You want people who would be eager
3 volunteers, because those are the people -- they may
4 differ from people who are not in the study in many
5 ways, but probably not in a biological features that we
6 are studying. But one way that they would differ is
7 that they would be more likely to stay with the study
8 and continue to give us information.

9 Another feature we discussed was the
10 possibility of using certain occupational groups as
11 primarily groups to recruit. That is something that
12 might be considered.

13 The last thing on my list is that we
14 talked about the importance of doing certain validation
15 studies on sub-samples of the cohort, so that we can
16 characterize exposure better.

17 DR. OWEN: Maybe I missed when you were
18 talking about features in terms of outcomes --

19 DR. ROTHMAN: Periodic contacts every six
20 months would be to not only get more exposure
21 information, but to screen of occurrence of certain
22 outcomes. Have you been hospitalized would be a
23 typical question and, if so, for what and if they were
24 hospitalized for cancer, then you want to get in touch
25 with them and find out how to get their medical

1 records, for example.

2 DR. OWEN: So, by that approach, then
3 perhaps you would not have to have a very tightly
4 defined set of outcomes that you were going to look at?

5 DR. ROTHMAN: You probably would. You
6 would have to have an action plan.

7 DR. OWEN: That is where I was trying to
8 get to is what sort of outcomes would we include?

9 DR. ROTHMAN: That is something that is
10 hard to do in a short time.

11 DR. OWEN: We talked about some of them.

12 DR. ROTHMAN: Right, probably any cancer.
13 As long as you are going to study cancer, study them
14 all. And I think most serious diseases that lead to
15 hospitalization would be worth studying, not because
16 you think of any of them as being related to cellular
17 telephone use, but they might be related to the other
18 exposures you are studying and in the end, it would be
19 valuable body of data anyway that would be acquired at
20 very little extra cost.

21 But you probably wouldn't want to include
22 everything. So, that would take a three-day conference
23 to figure out what outcomes to include and a lot of
24 shouting.

25 DR. MOULDER: I think you can say we are

1 talking about most if not all cancer outcomes, plus
2 some other outcomes, particularly some other
3 neurological outcomes. Also keeping in mind that one
4 of the great advantages of doing a cohort study is you
5 could always change your mind after you designed it and
6 either drop thing that turn out to be dull or add
7 things because of new information. Outcomes, that is.

8 DR. ROTHMAN: It's even possible to study
9 what many people think are soft outcomes like
10 schizophrenia by asking about certain kinds of
11 treatments. For example, have you been prescribed the
12 following drug or drugs and you can get information
13 that way, so there are certain treatments that are
14 specific for certain diseases and you can get the
15 outcome information by asking about the treatments.
16 Drug treatments particularly are useful for that.

17 So, Alzheimer's disease, schizophrenia and
18 other conditions like that, which may be hard to define
19 diagnostically --

20 DR. MOULDER: Well, Alzheimer's is usually
21 going to be a loss to follow up. You are going to have
22 to chase.

23 DR. ROTHMAN: That's why in the initial
24 questionnaire you want to get information on next of
25 kin and address and contact information, whom can we

1 contact at a different address if we can't find you.
2 These are all standard things to get in cohort studies.

3 DR. RINSKY: At the worst, it would be a
4 six-month trail rather than a 10-year trail.

5 DR. OWEN: Does anybody want to try to
6 pick out the things that we talked about earlier today
7 that don't fit into either of these two boxes that we
8 just hit -- the case control or the cohort? There are
9 some other -- and the particular type of case control
10 and this cohort.

11 DR. MOULDER: Well, the one occupational
12 one that was left on the table as possible was military
13 and I am not sure whether that would be a cohort or a
14 case control, because I don't have any idea who it
15 could be done. We identified that as the occupation
16 group that is most likely identifiable and most likely
17 to have high exposures.

18 DR. McBRIDE: If I can jump back and add a
19 little bit to Ken's list. As a further justification
20 for looking at modern technology, if we want to find a
21 broader hypothesis, again, not necessarily because
22 there is huge evidence that there are major health
23 effects from some of these technologies, but again, for
24 those technologies that are very prevalent in society -
25 - like videos, but it seems sufficient justification to

1 be looking for even small risks.

2 DR. OWEN: That is even largely
3 justification for looking at wireless phones in the
4 first place.

5 DR. McBRIDE: It is, so I would extend
6 that.

7 DR. ROTHMAN: You can study forced air
8 ventilation. There are a lot things you can add to it
9 -- environmental factors. And it would make sense to
10 do that. It's not really -- it really enhances the
11 study. If you can take the focus away from one or two
12 things that you are interested in, it helps.

13 DR. McBRIDE: I guess in order to limit
14 that list, one might want to focus on things that are
15 relatively new technologies and that are quite
16 prevalent and that are in use by the general population
17 and not just specific sub-groups in controlled
18 environments.

19 DR. OWEN: That would be another three-day
20 shouting match to pick those.

21 DR. ROTHMAN: A study like this, you need
22 a few sessions like that to go through a process of
23 narrowing down what you are going to do. And that
24 could occur before or after the final study team is put
25 together.

1 DR. OWEN: One other thing that I recall
2 that we touched on was to look at registries and screen
3 for things by looking at registries. There wasn't a
4 lot of discussion, but it was mentioned once or twice.

5 DR. MOULDER: Well, it's a relatively
6 obvious thing to do for cancers that have been stable
7 over time. There are some decent registries in this
8 country and I gather that is not a terribly expensive
9 sort of thing to do when the registry is already set
10 up.

11 DR. INSKIP: No, it's very easy to do.

12 DR. MOULDER: I think that is why we
13 didn't discuss it a lot, because it's an obvious thing
14 to do and a cheap thing to do.

15 DR. ROTHMAN: It's just a hard thing to
16 interpret.

17 DR. MOULDER: Yes.

18 DR. McBRIDE: Yes.

19 DR. MOULDER: It's not as hard to do if
20 you do it and find no change. What is hard to
21 interpret is changes.

22 DR. ROTHMAN: No, no change is hard to

23 interpret. We had an epidemic of endometrial cancer in
24 this country. It probably increased between five and
25 10 fold among people on post-menopausal estrogens and

1 yet the cancer registry showed no increase at all or
2 belatedly showed a small increase and how could they
3 miss a five or 10 fold increase in a segment of the
4 population that became proportionally very big? The
5 answer was at the same time, there was an increase in
6 hysterectomies and in the denominators and cancer
7 registries they hadn't figured out that they have to
8 take out of the denominator the women who didn't have
9 the target organ.

10 DR. MOULDER: So, are you arguing that
11 it's probably not worth following the registries?

12 DR. ROTHMAN: No, I didn't say that. I
13 just said it was hard to interpret.

14 DR. OWEN: Anything else? Looks like we
15 have run out of steam. Either that or the job is done.

16 DR. BALZANO: The only thing that I can
17 add again is that dosimetric shouldn't be
18 underestimated, especially with the proliferation of
19 devices that people use now to place the cell phone in
20 a variety of locations other than the head. You may be
21 looking for a variety of end points like you are
22 proposing here. The dosimetric part of the study is to

1 collected all your thoughts about the issues that you
2 wanted to address, you could circulate an e-mail and we
3 could add additional comments.

4 DR. OWEN: Yes, I think I will end up
5 doing that partly because having these two separate
6 meetings and having some people who we thought were
7 going to come and may not end up coming at all, so I
8 have already decided that I would have to try and get
9 something out of some people only by correspondence.
10 So, I think that is a good idea and I will try to do
11 that.

12 DR. MOULDER: Do you still want to have a
13 read back of your notes in the morning?

14 DR. OWEN: I don't think I have a choice
15 about whether we convene a meeting in the morning
16 because it was announced.

17 DR. MOULDER: If you want to spend some
18 hours tonight typing that up, we can critique your
19 words again in the morning.

20 DR. OWEN: That is pretty much what I see
21 remaining. Also, after overnight, people come up with
22 entirely new things that didn't happen to occur to them
23 today. Well, some people, a night's sleep makes a big
24 difference in new ideas.

25 DR. McBRIDE: I don't want to miss a point

1 that Ken referred to as well as Q. pointing out that we
2 do need some preliminary studies to look at the
3 exposure assessment issue. There does need to be some
4 preliminary work certainly in refining the design. The
5 IARC study took two or three years to come up with
6 their design and that may include some different ways
7 of collecting data. It's very important of course to
8 maximize the participation rate and the data
9 completeness and that will take some time in order to
10 come up with the best design.

11 DR. MOULDER: You could be designing the
12 cohort study and doing a preliminary dosimetry at the
13 same time. It's not one first and then the other.

14 DR. McBRIDE: Yes.

15 DR. MOULDER: Because the dosimetry is
16 going to tell you exactly what questions to ask.
17 Things still have to be set up, recruitment has to be
18 figured out, so it's not that you do all of one before
19 you start the other.

20 We were talking about using the web to
21 follow-up the patients -- patients -- but we could also
22 probably use the web very effectively to recruit for

23 this because various of us around this room control
24 websites where people who are interested in this
25 subject come. And once this is set up, a basic banner

1 ad could be made and go on things running from our
2 website that says this study has been created by so and
3 so, are you interested in participating, click through.

4 DR. ROTHMAN: You can have enrollment
5 extend over a period of a couple of years with no
6 problem, so you can be recruiting people gradually and
7 that way, I think you could put together a fairly good
8 cohort.

9 We shouldn't drop the idea entirely at
10 this stage of trying to recruit these occupational
11 groups with high exposures. If you could get into a
12 newsletter of real estate brokers and get their
13 organization to endorse the study, that would be good.

14 DR. MOULDER: They have their own web
15 sites.

16 DR. ROTHMAN: Yes, but they also probably
17 have newsletters and so forth. The ones that want to
18 will be the ones you want to get.

19 DR. MOULDER: If you do a web, you also
20 have to get web-friendly to start with or it's not
21 going to work.

22 DR. ROTHMAN: Right. Your idea of
23 referring to a web site to start with is great, but
24 they may get that referral from a printed page.

25 DR. OWEN: Yes, if you want to end up with

1 people who are going to be eager in this type of web
2 based query, you can use the web to find them and
3 recruit them and help weed out the ones who won't work
4 out.

5 DR. ROTHMAN: You have to have some mail
6 contact in the beginning, some postal contact, because
7 you have to make sure that you don't have fraudulent --

8 DR. MOULDER: Would you have to? If
9 either practical or epidemiologic purposes restrict us
10 to the US?

11 DR. ROTHMAN: That's a good question. I
12 think you would have difficulty in the outcome
13 assessment if you did not.

14 DR. MOULDER: I would tend to agree.

15 DR. McBRIDE: What about including Canada?
16 Would that still be true about the outcome assessment?

17 DR. ROTHMAN: I don't know. It might be.
18 You might have different methods then for that part of
19 the study. You wouldn't be able to go to the National
20 Death Index to look at deaths.

21 DR. McBRIDE: You would go to the National
22 Mortality Database.

23 DR. ROTHMAN: Yes, it might work fine. I
24 could easily imagine the US and Canada.
25 DR. INSKIP: Some of the Nordic countries

1 have pretty good cancer registries.

2 DR. McBRIDE: I think a records based
3 linkage study, which is a different --

4 DR. INSKIP: Well, you start --

5 DR. McBRIDE: On the other hand, for
6 outcome assessment, in Canada we do linkage studies to
7 hospital databases, mortality databases. If you had
8 sufficient identifiers and that is not just the
9 demographic identifiers, but some sort of recent
10 location identifier.

11 DR. ROTHMAN: Nordic countries are another
12 good suggestion because there is a lot of cell phone
13 use there and lots of web access, so it would be a nice
14 extension also.

15 DR. MOULDER: Clearly, that would have to
16 be decided very early in the game, what countries would
17 be allowed to come in.

18 DR. McBRIDE: I was thinking this was a US
19 study, but it is true that we have several national
20 health databases that can be used to identify outcomes,
21 rather than using self-reports or screening questions.

22 DR. RINSKY: Isn't there some special

23 confidentiality requirements of statistics in Canada
24 and won't let you link a name with a death certificate,
25 so that you can't use that? I don't know about the

1 other.

2 DR. McBRIDE: There are privacy and
3 confidentiality concerns, but there is a process by
4 which that linkage can take place and what is returned
5 to the investigator is the linked exposure outcome
6 records, individual records with the identifiers
7 stripped off so that you can analyze them
8 statistically.

9 DR. RINSKY: But if we were to find out in
10 follow-up that Mr. Smith passed probably of something
11 we might be interested in, we would have to submit 20
12 potential Mr. Smiths and we would get back -- without
13 ever knowing which one is the right one --

14 DR. McBRIDE: You can verify a death and a
15 cause of death on an individual record. That is done.

16 DR. RINSKY: Okay.

17 DR. McBRIDE: And the same for the Cancer
18 Institute's file.

19 DR. MOULDER: Would going out of the US
20 make loss to follow-up searches that much harder? The
21 person who this month is not there when you send the e-
22 mail -- in your own country, you know many more tricks

23 for finding people.

24 DR. ROTHMAN: It would be a big

25 complication. I'm not sure it's insuperable and it

1 might be worth it. I don't know. It's easier to
2 conceive of it as an in country study.

3 DR. OWEN: Could anyone help clarify for
4 me whether using the kind of web based follow-ups and
5 so on that we have been talking about, would that be
6 trail-blazing or has this been fairly well developed in
7 other studies?

8 DR. ROTHMAN: I think that by the time
9 this study would actually get under way, it would not
10 be trail-blazing, but if it were starting today, it
11 would be close.

12 DR. OWEN: So, there will be something --
13 or we can reasonably anticipate that there will soon be
14 some experience to build on.

15 DR. ROTHMAN: There already is some, but
16 not of this scope. That is what sets this apart.

17 DR. OWEN: So, it's mostly been kind of
18 more in a feasibility level and -- that the idea would
19 work, but it hasn't been used in any studies yet.

20 DR. ROTHMAN: The problem is I haven't
21 done any survey of what has gone on, but I think we
22 could find out.

23 DR. INSKIP: I think that has come up
24 before in the context of doing case control studies of
25 very rare cancers where there is not a national data

1 registry or any individual institutions have gone
2 through multiple centers, but to the extent that you go
3 through hospitals to identify people rather than self-
4 volunteering, I think there is a concern that you have
5 to do an IRB application at every one of 600,000
6 hospitals and that slows it, but that is a different
7 structure than what Ken has proposed here. I don't
8 know if IRBs would just want the home institution -- if
9 that would be the only relevant IRB for something like
10 this.

11 DR. MOULDER: Partly, it works together
12 very nice. As Ken suggests, this is pitched as a
13 cohort study of modern technology. Doing it with
14 modern technology would seem very appropriate and
15 actually make it an easier sell to the sort of people
16 you want to reach.

17 DR. OWEN: One of the reasons that that
18 question that I just asked came to mind was at
19 lunchtime, it occurred to me how often I have been in a
20 situation where I am doing something web based and then
21 my AOL connection drops off mysteriously in the middle
22 of whatever I am doing and thinking how if I was doing
23 my 10 or 15 minute questionnaire, how many times would
24 that have to happen before I got pretty fed up and
25 became non-compliant with the study.

1 DR. ROTHMAN: AOL could solve that problem
2 before the study starts.

3 DR. RINSKY: Think of this. Remember when
4 we began buying our own personal software. We would go
5 to great lengths to register. When was the last time
6 you even bothered registering on some software that you
7 bought? Just something that over the years you get
8 tired of and realize that it really doesn't have any
9 personal effect on you and you get busier in life and
10 things change.

11 So, you are going to need some way to get
12 back to these people and at some point when there is
13 their self-motivation wanes, there has got to be some
14 other way.

15 DR. MOULDER: I think we are heading
16 toward the time when people are going to be less and
17 less willing to fill out paper questionnaires. We are
18 already discovering that on some routine patient
19 follow-up. People are just used to doing it the new
20 way now and don't like to do it the old-fashioned way.

21 But we don't have a big confidentiality --
22 this still imaginary study does not pose the
23 confidentiality problems to the extent that medical
24 follow-up does. We are asking for some confidential
25 information, but --

1 DR. ROTHMAN: At some point, you have got
2 to get permission to look at medical records to verify
3 --

4 DR. MOULDER: No, I am thinking of the
5 kinds of problems that transmitting data over the
6 internet is hardly a fully confidential procedure at
7 the moment.

8 DR. ROTHMAN: Well, you could get a secure
9 website if you wanted.

10 DR. MOULDER: Would you need to?

11 DR. ROTHMAN: It might help compliance.

12 DR. MOULDER: Since we are asking people
13 about diseases, so it is medical information.

14 DR. ROTHMAN: I don't know how difficult
15 it is to set that up. I know it's done all the time.

16 DR. RINSKY: You may be asking questions
17 about income as well.

18 DR. MOULDER: You would want to ensure
19 them of internet confidentiality.

20 DR. BALZANO: I mean, people send over the
21 internet credit card numbers.

22 DR. OWEN: But again, if you are sort of
23 trying to gradually sift through and select for the
24 people that are going to be your best responders down
25 the road, you probably also are going to be dealing

1 with people who have spent time sending confidential
2 information over the web either through credit card
3 purchases or I have noticed that half the websites you
4 go to they ask you how much money you make and how many
5 people in your family and what you drive.

6 DR. MOULDER: Do you tell them?

7 DR. OWEN: I make up answers.

8 DR. ROTHMAN: You give them what you wish
9 you made rather than what you do.

10 DR. BALZANO: You send to each different
11 answers and confuse them both.

12 DR. RINSKY: I guess a serious question in
13 that regard though, is there any difficulty with
14 generalizing from that kind of population of type A
15 people who like to work on computers to the general
16 population?

17 DR. ROTHMAN: I think the short answer is
18 no.

19 DR. RINSKY: You are satisfied then?

20 DR. OWEN: And if the answer is yes, it's
21 probably becoming less so.

22 DR. ROTHMAN: Well, there is this mistaken

23 notion in epidemiology on the part of some people that
24 generalization depends upon just statistical sampling
25 characteristics of the study group as if every

1 epidemiologic study was done like a Gallup pole or a
2 survey, but that I really not what is at issue for
3 generalization. Generalization is really testing the
4 scientific relationship.

5 In this case, we would be investigating
6 biological hypotheses and the question is would the
7 biology of the people you are studying be different
8 from the biology of people not in your study?

9 It is certainly possible. It's just not
10 really that plausible.

11 DR. MOULDER: The risk factors various
12 things may be different from the rest of the
13 population, but if you design the study right, that
14 falls out.

15 DR. OWEN: Okay, it's about five until
16 5:00 and I will stick with that plan of trying to
17 reorganize what I think I have heard today in
18 order to
19 elicit clarification or extension of those
20 things
21 tomorrow morning.

22 Because it's difficult for local
23 people to
24 get here as early as 8:00, if everybody that is
25 here

22 right now thinks it's okay, I think we could
start at

23 8:30 instead of 8:00 and still have plenty of
time left

24 on our agenda. Anybody think that will be a
problem?

25 Okay.

2 your evening and see you tomorrow.

 (Whereupon, at 4:52 p.m. the meeting
adjourned, to reconvene at 8:30 a.m. April 19,
2001.)

* * * * *

REPORTER'S CERTIFICATE

I, Laurie McClung, reporter, hereby certify that the foregoing transcript consisting of 222 pages is a complete, true, and accurate transcript of the meeting, held on April 18th, 2001 at the Regal Cincinnati Hotel, Cincinnati, Ohio.

I further certify that this proceeding was recorded by me, and that the foregoing transcript has been prepared under my direction.

Date: May 4, 2001

Official Reporter

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